Subject: Ablation of Liver Tumors
Policy Number: NMP124
Effective Date*: March 2004
Updated: February 2016

This National Medical Policy is subject to the terms in the
IMPORTANT NOTICE
at the end of this document

For Medicaid Plans: Please refer to the appropriate State’s Medicaid
manual(s), publication(s), citation(s), and documented guidance for
coverage criteria and benefit guidelines prior to applying Health Net
Medical Policies

The Centers for Medicare & Medicaid Services (CMS)
For Medicare Advantage members please refer to the following for coverage
guidelines first:

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Instructions
- Medicare NCDs and National Coverage Manuals apply to ALL Medicare members in ALL regions.
- Medicare LCDs and Articles apply to members in specific regions. To access your specific region, select the link provided under “Reference/Website” and follow the search instructions. Enter the topic and your specific state to find the coverage determinations for your region. *Note: Health Net must follow local coverage determinations (LCDs) of Medicare Administration Contractors (MACs) located...
outside their service area when those MACs have exclusive coverage of an item or service. (CMS Manual Chapter 4 Section 90.2)

- If more than one source is checked, you need to access all sources as, on occasion, an LCD or article contains additional coverage information than contained in the NCD or National Coverage Manual.
- If there is no NCD, National Coverage Manual or region specific LCD/Article, follow the Health Net Hierarchy of Medical Resources for guidance.

Current Policy Statement
Health Net, Inc. considers radiofrequency ablation (RFA) of liver tumors medically necessary for any of the following:

**A. Primary Hepatocellular Carcinoma (HCC)**
1. Primary or recurrent hepatocellular carcinoma in an adult patient with all of the following:
   - The procedure is being performed with curative intent in treating tumors ≤3cm (not palliation which is considered experimental and investigational); or
   - No pre-procedural or intraoperative evidence of extrahepatic disease; or
   - No tumor size > 5 cm in diameter; or
   - Surgical resection of the entire tumor is not possible because of extent and/or location near major intrahepatic blood vessels precluding a margin-negative resection, multifocality, or inadequate hepatic function related to coexistent cirrhosis; or

2. As an adjunct to surgical resection to assure complete ablation of the desired lesion(s) with curative intent; or

3. Initial and recurrent liver metastases of carcinoid tumors in patients with carcinoid syndrome (abdominal cramps, diarrhea, wheezing and flushing of the skin); or

4. Limited hepatic reserve and cirrhosis preventing a patient from having a portion of his/her liver removed.

**B. Metastatic Liver Tumor**
1. Liver metastasis from primary colorectal cancer * when all of the following are met:
   - RFA is being performed with intent to remove all visible tumor, not palliation which is considered investigational; and
   - Patient has asymptomatic disease other than any symptoms that could be attributed to the hepatic lesions; and
   - The primary cancer site must be effectively controlled by prior curative resection; and
   - All tumors would be potentially destroyed by RFA; and
   - The metastatic lesions must be limited to the liver and not present in other organs;
- No tumor should be larger than 5 cm in size; and (7cm Medicare)
- The patient must have no more than 3 liver metastases, as documented by an pre-procedure CT / MRI; and
- Tumor occupies < 50% of the liver parenchyma; and
- Because open surgical resection is the preferred treatment, comorbid medical conditions must preclude open surgical resection.

2. Patients with benign tumors such as focal nodular hyperplasia and adenomas

Note: Radiofrequency ablation can be administered by open surgery, laparoscopic surgery or percutaneous.

Note: For metastases to the liver from primary carcinomas of the breast, lung, stomach, pancreas, adenoacarcinomas of unknown origin, and other such primary sites that tend to be disseminated widely at the same time that liver metastases are present, ablation by RFA is considered investigational. Although clinical trials continue to be done, the scientific evidence and outcomes are inconclusive.

**Percutaneous Ethanol Injection (PEI)**

Health Net, Inc. considers chemical ablation or percutaneous ethanol injection (PEI) for unresectable primary, localized hepatocellular liver cancer (HCC) medically necessary when both of the following criteria are met:

- Tumors are < 5cm in diameter; and
- Tumor is encapsulated, with well defined margins, and not located near the surface of the liver.

**Definitions**

- HCC  Hepatocellular Carcinoma
- RFA  Radiofrequency ablation
- PEI  Percutaneous Ethanol Injection
- TACE  Transarterial chemoembolization
- OLT  Orthotopic liver transplantation
- CRHM  Hepatic metastases from colorectal cancer
- CLOCC  Cancer Chemotherapy + Local Ablation Versus Chemotherapy
- LITT  Laser-induced thermotherapy
- MWA  Microwave ablation
- OS  Overall survival
- PFS  Progression free survival
- CRC  Colorectal cancer
- NCLM  Non-colorectal liver metastasizes

**Codes Related To This Policy**

**ICD-9 Codes**

NOTE:
The codes listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service described by this code is a covered or non-
covered health service. Coverage is determined by the benefit documents and medical necessity criteria. This list of codes may not be all inclusive.

On October 1, 2015, the ICD-9 code sets used to report medical diagnoses and inpatient procedures have been replaced by ICD-10 code sets.

**ICD-9 Codes**

152.0-152.2 Malignant neoplasm of small intestine, including duodenum, jejunum, ileum
152.8 Malignant neoplasm of small intestine, other specified sites of small intestine
152.9 Malignant neoplasm of small intestine, small intestine, unspecified
153.0-153.9 Malignant neoplasm of colon
154.0-154.8 Malignant neoplasm of rectum, recto sigmoid junction, and anus
155.0-155.1 Malignant neoplasm of liver, primary
156.0 Malignant neoplasm of gall bladder
182.0 Malignant neoplasm of corpus uteri, except isthmus [endometrial]
183.0 Malignant neoplasm of ovary
197.7 Secondary malignant neoplasm of liver
198.82 Secondary malignant neoplasm of genital organs
259.2 Carcinoid syndrome

**ICD-10 Codes**

C17.0-C17.9 Malignant neoplasm of small intestines
C18.0-C18.9 Malignant neoplasm of colon
C19 Malignant neoplasm of rectosigmoid junction
C20 Malignant neoplasm of rectum
C21.0-C21.8 Malignant neoplasm of anus and anal canal
C22.0-C22.9 Malignant neoplasm of liver and intrahepatic bile ducts
C23 Malignant neoplasm of gallbladder
C78.7 Secondary malignant neoplasm of liver and intrahepatic bile duct
E34.0 Carcinoid syndrome

**CPT Codes**

47370 Laparoscopy, surgical, ablation of one or more liver tumor(s); radiofrequency
47380 Ablation, open, of one or more liver tumor(s); radiofrequency
47382 Ablation, 1 or more liver tumor(s), percutaneous, radiofrequency
49203 Excision or destruction, open, intra-abdominal tumors, cysts or endometriomas, 1 or more peritoneal, mesenteric, or retroperitoneal primary or secondary tumors; largest tumor 5 cm diameter or less
49204 Excision or destruction, open, intra-abdominal tumors, cysts or endometriomas, 1 or more peritoneal, mesenteric, or retroperitoneal primary or secondary tumors; largest tumor 5.1 -10.0 cm diameter
49205 Excision or destruction, open, intra-abdominal tumors, cysts or endometriomas, 1 or more peritoneal, mesenteric, or retroperitoneal primary or secondary tumors; largest tumor > 10cm.
76940 Ultrasound guidance for, and monitoring of, visceral tissue ablation
77013 Computerized tomography guidance for, and monitoring of, parenchymal tissue ablation
77022 Magnetic resonance guidance for, and monitoring of, parenchymal tissue ablation

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HCPCS Codes
N/A

Scientific Rationale – Update February 2016
The NCCN Guidelines (Version1.2016) on Hepatobiliary Cancers Update notes that the following bullet under ablation was removed:

“Sorefenib may be appropriate following ablative herapy in patients with adequate liver function once bilirubin returns to baseline if there is evidence of residual/recurrent tumor not amenable to additional local therapies. The safety and efficacy of adjuvant sorafenib following ablation is being investigated in an ongoing clinical trial”. NCCN replaced this with “Sorafenib should not be used as adjuvant therapy post-ablation.”

Scientific Rationale – Update February 2015
Lei et al. (2014) completed a study to compare the effectiveness and safety of hepatic resection and radiofrequency ablation (RFA) for small hepatocellular carcinomas (HCCs) less than 5cm in diameter. A total of 289 patients were diagnosed with a small HCC (a single tumor no larger than 5cm). Among these patients, 133 underwent hepatic resection, and 156 received RFA. Demographic data, intraoperative data, post-operative recovery data, and the baseline characteristics of the 2 groups of patients were compared. The incidence of post-operative complications; 1-, 3-, and 5-year survival rates; and tumor recurrence were determined. No statistically significant differences in the baseline characteristics were noted between the 2 groups. By contrast, operation time (P=0.003), intraoperative blood loss (P=0.000), and the length of post-operative hospital stay (P=0.000) were significantly lower in the RFA group compared with the surgical resection group. The 2 groups displayed similar post-operative complication rates (12% or 16/133 in the liver resection group vs. 8.3% or 13/156 in the RFA group, P=0.395). The 1-, 3-, and 5-year overall survival rates of the patients in the liver resection group were 88.7%, 78.2%, and 66.2%, respectively, whereas the rates in the RFA group were 90.4%, 76.3%, and 66.0%, respectively (P=0.722). The 1-, 3-, and 5-year tumor-free survival rates of patients in the resection group were 87.2%, 69.9%, and 58.6%, respectively, whereas the rates in the RFA group were 85.9%, 66.0%, and 54.5%, respectively (P=0.327). In addition, among HCC patients receiving RFA, patients with tumors no greater than 3cm in diameter exhibited no significant differences regarding overall survival and tumor-free survival rates compared with patients with tumors 3 to 5cm in diameter (all P>0.05). RFA is an effective and safe treatment option for small HCCs and may be a preferred choice for HCC patients with small lesions.

Scientific Rationale – Update February 2014
Oiu et al (2013) assessed the perioperative outcomes, recurrence, and long-term survival rates for patients treated with hepatic resection (HRE) plus radiofrequency ablation (RFA) in the management of primary hepatocellular carcinoma (HCC) and metastatic liver cancer (MLC). Data from all consecutive patients with primary and secondary hepatic malignancies who were treated with HRE combined with RFA between 2007 and 2013 were prospectively collected and retrospectively reviewed. A total of 112 patients, with 368 hepatic tumors underwent HRE combined with ultrasound-guided RFA, were included in the present study. There were 40 cases of HCC with 117 tumors and 72 cases of MLC with 251 metastases. Most cases of liver
metastases originated from the gastrointestinal tract (44, 61.1%). Other uncommon lesions included breast cancer (5, 6.9%), pancreatic cancer (3, 4.2%), lung cancer (4, 5.6%), cholangiocarcinoma (4, 5.6%), and so on. The ablation success rates were 93.3% for HCC and 96.7% for MLC. The 1-, 2-, 3-, 4-, and 5-y overall recurrence rates were 52.5%, 59.5%, 72.3%, 75%, and 80% for the HCC group and 44.4%, 52.7%, 56.1%, 69.4%, and 77.8% for the MLC group, respectively. The 1-, 2-, 3-, 4-, and 5-y overall survival rates for the HCC patients were 67.5%, 50%, 32.5%, 22.5%, and 12.5% and for the MLC patients were 66.5%, 55.5%, 50%, 30.5%, and 19.4%, respectively. The corresponding recurrence-free survival rates for the HCC patients were 52.5%, 35%, 22.5%, 15%, and 10% and for the MLC patients were 58.3%, 41.6%, 23.6%, 16.9%, and 12.5%, respectively. Reviewers concluded that HRE combined with RFA provides an effective treatment approach for patients with primary and secondary liver malignancies who are initially unsuitable for radical resection, with high local tumor control rates and promising survival data.

Zhou et al (2013) compared the short-term and long-term outcomes of resection and RFA in cases of very early HCC (tumors<2 cm in diameter). Between July 2003 and August 2008, 52 patients were diagnosed as very early HCC (≤2 cm), of whom 21 received a liver resection and 31 underwent RFA. We compared the baseline characteristics, the intraoperative data, and the recovery metrics between these two groups including postoperative complications and the 1-, 3-, and 5-year overall and tumor-free survival rates. No statistically significant differences were observed in the baseline characteristics between very early HCC patients allocated to the liver resection group and those in the RFA group. The liver function in the liver resection group was better than that of the RFA group with respect to the Child score (P=0.004), but not the model for end-stage liver disease score (P=0.066). More tumor targets were located in the center of the liver (compared with the periphery) in the RFA group (P=0.003). The RFA patients showed much shorter operative times, less blood loss, and had shorter hospital stays than the resection group but had a much higher overall cost (all P=0.000). The 1-, 3-, and 5-year overall survival rates were 95.2, 85.7, and 81.0%, respectively, for the liver resection group, and 93.5, 90.3, and 80.6%, respectively, for the RFA group (P=0.976). The 1-, 3-, and 5-year tumor-free survival rates were 90.5, 81.0, and 76.2%, respectively, in the resection group and 90.3, 83.9, and 71.0%, respectively, in the RFA group (P=0.830). Investigators concluded with comparable short-term and long-term effects on overall survival and tumor recurrence rate and with a shorter operative time, less blood loss, and a shorter hospital stay, RFA should be considered as the first choice for the treatment for very early HCCs as it presents an efficacious and economic option.

**Scientific Rationale – Update February 2013**

Per the National Comprehensive Cancer Network (NCCN) guidelines on Hepatocellular Carcinoma (2012):

"Following an initial workup for hepatocellular cancer (HCC), patients are stratified into one of the following 4 categories:

- Potentially resectable or transplantable, operable by performance status or comorbidity
- Unresectable disease
- Inoperable by performance status or comorbidity with local disease only
- Metastatic disease

All HCC patients should be evaluated for potential curative therapies (resection, transplantation). Those patients not candidates for curative treatments may be
treated with locoregional approaches. These are broadly categorized into ablation and transarterial embolization.

Selection criteria for ablative therapy include patients with local disease only characterized as being completely amenable to ablative therapy according to size and location of the tumor(s).

Ablation (radiofrequency, cryoablation, percutaneous alcohol injection, microwave):
- All tumors should be amenable to ablation such that the tumor and margin of normal tissue is treated.
- Tumors should be in a location accessible for percutaneous/laparoscopic/open approached for ablation.
- Tumors ≤ 3 cm are optimally treated with ablation. Lesions between 3-5 cm may be treated using combination embolization and ablation as long as tumor location is favorable. Unresectable/inoperable lesions >5 cm should be considered for treatment using arterial embolic approaches or systemic therapy.
- Caution should be exercised when ablating lesions near major vessels, major bile ducts, diaphragm, and other intra-abdominal organs.
- Sorafenib is appropriate for post ablation therapy in patients with adequate liver function once bilirubin returns to baseline if there is evidence of residual/recurrent tumor not amenable to additional local therapies. The safety and efficacy of the use of sorafenib concomitantly with ablative procedures is being investigated in ongoing clinical trials.”

Solbiati et al (2012) sought to determine the long-term (10-year) survival of patients with colorectal liver metastases treated with radiofrequency (RF) ablation and systemic chemotherapy with intention to treat. From 1997 to 2006, 99 consecutive patients with 202 small (0.8-4.0 cm; mean: 2.2 cm ± 1.1) metachronous colorectal liver metastases underwent ultrasonography-guided percutaneous RF ablation with internally-cooled electrodes in association with systemic chemotherapy. Patients ineligible for surgery (n = 80) or whose lesions were potentially resectable and who refused surgery (n = 19) were included. Patients were followed up with contrast agent-enhanced computed tomography and/or magnetic resonance imaging for a minimum of 3 years to more than 10 years after RF ablation (n = 99, 67, 49, and 25 for 3, 5, 7, and 10 or more years, respectively). Overall local response rates and long-term survival rates were assessed. For each of these primary endpoints, Kaplan-Meier curves were generated and log-rank tests were used to assess for statistically significant differences. Primary and secondary technical success rates were 93.1% (188 of 202) and 100% (14 of 14), respectively. Local tumor progression occurred in 11.9% (24 of 202) metastases, and 54.2% (13 of 24) of these were re-treated. Patient survival rates increased with re-treatment versus no re-treatment (P < .001). At follow-up, 125 new liver metastases were found, and of these 32.8% (41 of 125) were treated with RF ablation. Overall survival rates were 98.0%, 69.3%, 47.8%, 25.0%, and 18.0% (median: 53.2 months) at 1, 3, 5, 7, and 10 years, respectively. The major complication rate was 1.3% (two of 156), and there were no procedure-related deaths. At the time this article was written, 32.3% (32 of 99) of the patients were alive, and 67.7% (67 of 99) were deceased, with a median follow-up of 72 months. Authors concluded adding RF ablation to systemic chemotherapy achieved local control in a large majority of metachronous colorectal liver metastases. The 3- to 10-year survival rates of this relatively large series of patients were essentially equivalent to those of most surgical series reported in the literature.
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Vogl et al (2012) reviewed studies on RFA, laser-induced thermotherapy (LITT) and microwave ablation (MWA) regarding local tumor response, progression and survival indexes in patients with breast cancer liver metastases (BCLM). The reviewed literature showed positive response rates of 63 % to 97 % in RF-ablated lesions, 98.2 % in LITT-treated lesions and 34.5-62.5 % in MW-ablated lesions. Median survival was 10.9-60 months using RFA, 51-54 months after LITT and 41.8 months using MWA. Five-year survival rates were 27-30 %, 35 % and 29 %, respectively. Local tumour progression ranged from 13.5 % to 58 % using RFA, 2.9 % with LITT and 9.6 % with MWA. Investigators concluded the reviewed literature demonstrated that ablation therapies either as single therapy or combined with other locoregional therapies are a good alternative as an adjunction to resection in patients with resectable lesions or with positive response using chemotherapy. However, multicentre randomized studies should be conducted to obtain further evidence of the benefits of these treatments in patients with BCLM.

Le et al (2012) compared outcomes of patients with HCC who underwent surgical resection with those who received RFA. Using the Surveillance, Epidemiology, and End Results registry, they identified 1209 (21%) and 4595 (79%) patients with HCC who received RFA and surgical resection, respectively, between the years 1988 and 2008. When comparing the groups, patients undergoing RFA were older (years, 62.6 vs 58.7) and had smaller tumors (less than 5 cm; 84.4 vs 61.2%), yet patients who underwent surgical resection had improved survival over patients undergoing RFA (median survival, 5 vs 3 years, respectively). Univariate and multivariate analysis verified the superiority of surgical resection over ablation. They concluded their investigation demonstrates that surgical resection provides durable long-term survival for surgical candidates with HCC; however, RFA remains an appropriate alternative therapy that also provides long-term survival in select patients.

Ruers et al (2012) investigated the possible benefits of RFA in patients with non-resectable colorectal liver metastases. This phase II study, originally started as a phase III design, randomly assigned 119 patients with non-resectable colorectal liver metastases between systemic treatment (n = 59) or systemic treatment plus RFA (± resection) (n = 60). Primary objective was a 30-month overall survival (OS) rate >38% for the combined treatment group. The primary end point was met, 30-month OS rate was 61.7% for combined treatment. However, 30-month OS for systemic treatment was 57.6%, higher than anticipated. Median OS was 45.3 for combined treatment and 40.5 months for systemic treatment. PFS rate at 3 years for combined treatment was 27.6% compared with 10.6% for systemic treatment only. Median progression-free survival (PFS) was 16.8 months and 9.9 months, respectively. Investigators concluded the study met the primary end point on 30-month OS; however, the results in the control arm were in the same range. RFA plus systemic treatment resulted in significant longer PFS. At present, the ultimate effect of RFA on OS remains uncertain.

Veltri et al (2012) reviewed some prognostic factors for survival after RFA of metastases from colorectal cancer (CRC). From 1996 to 2009, 262 patients with metastases from CRC were treated with RFA. Fourteen were lost to follow-up. The following predictors were analysed in the remaining 248: synchronous/metachronous metastases, single/multiple metastases, diameter of largest metastasis and absence/presence of extrahepatic metastases. Survival was measured from the date of metastasis diagnosis and from the date of RFA. Survival at 1, 2, 3 and 5 years was 93%, 78%, 62% and 35% from metastasis diagnosis, and 84%, 59%, 43% and
23% from the date of RFA. Median survival was 41 months in patients with largest metastasis ≤3 cm and 21.7 months for those with metastases >3 cm; survival increased to 45.2 months in patients with largest metastasis ≤2.5 cm and fell to 18.5 months in those with metastasis >3.5 cm. Median survival of patients with extrahepatic metastases was significantly lower than that of patients without extrahepatic disease (23.3 vs. 32.6 months). Investigators concluded small lesion size (diameter of largest lesion ≤3 or 2.5 cm) proved to be the most favourable prognostic factor for survival in patients with CRC metastases to the liver treated with RFA. This conclusion is probably related to the possibility of obtaining radical ablation and points to the usefulness of devices allowing ablation of larger volumes. In the presence of extrahepatic metastases, RFA has less impact on survival, even though it is potentially useful in patients at a higher risk of death due to hepatic rather than extrahepatic metastases.

Treska et al (2012) evaluated the single center experience with surgical treatment of non-colorectal liver metastasizes (NCLM). Seventy two patients were prospectively included. The average length of time after the primary surgery was 3.9 years (0-8.5 years). RFA prevailed -50 patients (69.4%), resection presenting 30.6%. Preoperative chemotherapeutical downstaging or portal vein embolization was performed on 12 patients (16.7%). Resectable or radiofrequency ablation (RFA) treatable extrahepatic metastasizes were removed in 26 patients (36.1%). One, three and five years patient survival after the liver resection or RFA was 88.6, 72.5 and 36.9%. The best survival rate was in patients with carcinoid (5 years-100%), breast cancer (5 years-33.8%), renal carcinoma (3 years-44.4%) and gynecological tumors metastasizes (2 years-72.9%). With regards to long-term survival of patients, we did not find any statistically significant difference between RFA and resection. Patients with extrahepatic metastasizes had worse prognosis. Investigators concluded liver resection and RFA in NCLM have an unambiguous place in multi-modal curative strategy. The decision for surgical treatment of patients suffering from NCLM, is strictly individual with the aim of achieving qualitative long-term survival.

De Baere (2012) reported median survival after the first radiofrequency of a liver metastasis of CRC is reported to be 24 to 52 months with a 5 years overall survival of 18 to 44%. The median overall survival increases from 22 to 48 months depending on the use of radiofrequency ablation as rescue treatment after failure of others, or as a first line treatment. For patients with a single tumor, less than 4 cm, the survival rates at 1, 3, and 5 years are respectively 97%, 84% and 40%, with a median survival of 50 months.

There continues to be a paucity of data in the peer review literature evaluating the use of RFA of liver metastases from primary carcinomas of sites other than colon & rectum (e.g. breast, lung, stomach, pancreas etc).

**Scientific Rationale – Update September 2012**

Peng et al (2012) compared retrospectively the effects of percutaneous RFA with those of hepatic resection in the treatment of hepatocellular carcinoma (HCC) measuring 2 cm or smaller. From December 2003 to December 2008, 145 patients with a resectable HCC measuring 2 cm or smaller were studied. Sixty-six patients had a central HCC (located at least 3 cm from the liver capsule). As an initial treatment, 71 patients were treated with percutaneous RF ablation and 74 with surgical resection. Of the patients with central HCC, 37 underwent percutaneous RFA and 29 underwent surgical resection. Survival curves were constructed with the
Kaplan-Meier method and compared by using the log-rank test. The relative prognostic significance of the variables for predicting overall survival rates was assessed with multivariate Cox proportional hazards regression analysis. Complications were observed clinically when patients were admitted and assessed by telephone interview after patients were discharged.

One death was considered to be related to treatment after surgical resection. Major complications occurred significantly more often in the surgical resection group (38 of 74 patients) than in the RF ablation group (14 of 71 patients). The 1-, 3-, and 5-year overall survival rates were 98.5%, 87.7%, and 71.9%, respectively, with RF ablation and 90.5%, 70.9%, and 62.1% with surgical resection. The corresponding recurrence-free survival rates were 76.4%, 65.2%, and 59.8% with RF and 75.6%, 56.1%, and 51.3% with surgical resection. At subgroup analysis of patients with central HCC, 1-, 3-, and 5-year overall survival rates were 96.6%, 93.0%, and 79.9% with RF and 92.0%, 71.6%, and 61.5% with surgical resection. The corresponding recurrence-free survival rates were 86.5%, 74.0%, and 67.0% with RF and 68.0%, 40.0%, and 40.0% with surgical resection. For patients with peripheral HCC, 1-, 3-, and 5-year overall survival rates were 97.3%, 83.3%, and 65.1% with RF ablation and 87.8%, 68.4%, and 62.9% with surgical resection. The corresponding recurrence-free survival rates were 68.7%, 59.2%, and 54.9% with RF and 82.9%, 66.6%, and 52.9% with surgical resection. Investigators concluded the efficacy and safety of percutaneous RF were better than those of surgical resection in patients with HCC measuring 2 cm or smaller, especially those with central HCC.

Nishikawa et al (2011) compared the outcome of percutaneous RF (PRFA) with surgical resection (SR) in the treatment of single and small HCC. A retrospective cohort study was conducted on 231 treatment naive patients with a single HCC ≤ 3 cm who had received either curative PRFA (162 patients) or curative SR (69 patients). All patients were regularly followed up after treatment with blood and radiologic tests. The 1-, 3- and 5-year overall survival rates after PRFA and SR were 95.4%, 79.6% and 63.1%, respectively in the RFA group and 100%, 81.4% and 74.6%, respectively in the SR group. The corresponding recurrence free survival rates at 1, 3 and 5 years after PRFA and SR were 82.0%, 38.3% and 18.0%, respectively in the PRFA group and 86.0%, 47.2% and 26.0%, respectively in the SR group. In terms of overall survival and recurrence free survival, there were no significant differences between these two groups. In comparison of PRFA group patients with liver cirrhosis (LC) (n = 127) and SR group patients with LC (n = 50) and in comparison of PRFA group patients without LC (n = 35) and SR group patients without LC (n = 19), there were also no significant differences between two groups in terms of overall survival and recurrence free survival. In the multivariate analysis of the risk factors contributing to overall survival, serum albumin level was the sole significant factor. In the multivariate analysis of the risk factors contributing to recurrence free survival, presence of LC was the sole significant factor. The rate of serious adverse events in the SR group was significantly higher than that in the PRFA group. Hospitalization length in the SR group was significantly longer than in the PRFA group. Reviewers concluded PRFA is as effective as SR in the treatment of single and small HCC, and is less invasive than SR. Therefore, PRFA could be a first choice for the treatment of single and small HCC.

Peng et al (2012) prospectively compared the effects of RFA after TACE with those of RF ablation alone in the treatment of recurrent HCC. 139 patients with recurrent HCC measuring 5 cm in diameter or smaller were randomized to receive either sequential TACE and RF ablation (sequential treatment group, n=69) or RF ablation alone (RF
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ablation group, n=70). The survival curves were constructed with the Kaplan-Meier method and compared by using the log-rank test. Bonferroni correction was applied when multiple comparisons were performed. P<.0083 (.05÷6) was considered indicative of a statistically significant difference. The 1-, 3-, and 5-year overall survival rates were 94%, 69%, and 46%, respectively, for the sequential treatment group and 82%, 47%, and 36% for the RF ablation group. The corresponding recurrence-free survival rates were 80%, 45%, and 40% for the sequential treatment group and 64%, 18%, and 18% for the ablation group. At subgroup analyses, the overall survival for the sequential treatment group was better than that for the RF ablation group for patients with tumor recurrence 1 year or less after initial treatment and those with tumors measuring 3.1-5.0 cm but not for those with tumor recurrence more than 1 year after initial treatment and those with tumors 3.0 cm or smaller. The recurrence-free survival in the sequential treatment group was better than that in the RF ablation group for patients with tumors measuring 3.1-5.0 cm but not for those with tumors 3.0 cm or smaller. For recurrence-free survival, there was no significant difference between the two groups for patients with tumor recurrence 1 year or less or more than 1 year after initial treatment. Logistic regression analysis showed that treatment allocation and the interval between initial treatment and tumor recurrence were significant prognostic factors for overall survival, whereas the interval between initial treatment and tumor recurrence, treatment allocation, and tumor size were significant prognostic factors for recurrence-free survival. Investigators concluded the efficacy of sequential TACE-RF ablation is better than that of RF ablation alone for recurrent HCC.

Li et al (2012) evaluated the evidence comparing RFA and surgical resection (RES) on the treatment of HCC using meta-analytical techniques. A literature search was undertaken to identify comparative studies evaluating survival rates, recurrence rates, and complications. Pooled odds ratios (OR) and 95% confidence intervals (95% CI) were calculated with either the fixed or random effect model. These studies included a total of 877 patients: 441 treated with RFA and 436 treated with RES. The overall survival was significantly higher in patients treated with RES than RFA at 1, 3 and 5 years (respectively: OR: 0.50, 95% CI: 0.29-0.86; OR: 0.51, 95% CI: 0.28-0.94; OR: 0.62, 95% CI: 0.45-0.84). In the RES group the 1, 3, and 5 years recurrence-free survival rates were significantly higher than the RFA group (respectively: OR: 0.65, 95% CI: 0.44-0.97; OR: 0.65, 95% CI: 0.47-0.89; OR: 0.52, 95% CI: 0.35-0.77). RFA had a higher rate of local recurrence (OR: 4.08, 95% CI: 2.03-8.20). For tumors ≤ 3 cm RES was better than RFA in the 3-year overall survival rates (OR: 0.38, 95% CI: 0.16-0.89). Investigators concluded surgical resection was superior to RFA in the treatment of HCC. However, the findings have to be carefully interpreted due to the lower level of evidence.

Scientific Rationale – Update October 2011

Per the National Comprehensive Care Network (NCCN, 2011), Sorafenib was added as appropriate for post transcatheter arterial chemoembolization (TACE) / ablation therapy in patients with adequate liver function once bilirubin returns to baseline if there is evidence of residual / recurrent tumor not amenable to additional local therapies. The safety and efficacy of the use of sorafenib concomitantly with TACE / ablative procedures is being investigated in ongoing clinical trials.

Rossi et al. (2011) retrospectively analyzed a prospective series of 706 patients with cirrhosis (Child-Pugh class≤B7) who underwent RFA for 859 HCC≤35 mm in diameter (1-2 per patient). The results of RFA were classified as complete responses (CRs) or treatment failures. CRs were obtained in 849 nodules (98.8%) and 696...
patients (98.5%). During follow-up (median, 29 months), 465 (66.8%) of the 696 patients with CRs experienced a first recurrence at an incidence rate of 41 per 100 person-years (local recurrence 6.2; nonlocal 35). Cumulative incidences of first recurrence at 3 and 5 years were 70.8% and 81.7%, respectively. RFA was repeated in 323 (69.4%) of the 465 patients with first recurrence, restoring disease-free status in 318 (98.4%) cases. Subsequently, RFA was repeated in 147 (65.9%) of the 223 patients who developed a second recurrence after CR of the first, restoring disease-free status in 145 (98.6%) cases. Overall, there were 877 episodes of recurrence (1-8 per patient); 577 (65.8%) of these underwent RFA that achieved CRs in 557 (96.5%) cases. No procedure-related deaths occurred in 1,921 RFA sessions. Estimated 3- and 5-year overall and disease-free (after repeated RFAs) survival rates were 67.0% and 40.1% and 68.0 and 38.0%, respectively. RRFA is safe and effective for managing HCC in patients with cirrhosis, and its high repeatability makes it particularly valuable for controlling intrahepatic recurrence.

Primary lung cancers themselves most commonly metastasize to the adrenal glands, liver, brain, and bone. There is no mention in ‘NCCN’ or in the ‘American Association of Liver Disease’ guidelines, that RFA is indicated for metastases to the liver from primary carcinomas of the breast, lung, stomach, pancreas, adenocarcinoma of unknown origin, or other such primary sites.

Wong et al. (2009) The American Society of Clinical Oncology (ASCO) analyzed a comprehensive systematic review of the RFA literature from Medline and the Cochrane Collaboration Library. Because data were considered insufficient to form the basis of a practice guideline, ASCO has instead published a clinical evidence review. The evidence is from single-arm, retrospective, and prospective trials. No randomized controlled trials have been included. The following three clinical issues were considered by the panel: the efficacy of surgical hepatic resection versus RFA for resectable tumors; the utility of RFA for unresectable tumors; and RFA approaches (open, laparoscopic, or percutaneous). Evidence suggests that hepatic resection improves overall survival (OS), particularly for patients with resectable tumors without extrahepatic disease. RFA investigators report a wide variability in the 5-year survival rate (14% to 55%) and local tumor recurrence rate (3.6% to 60%). The reported mortality rate was low (0% to 2%), and the major complications rate was commonly reported to be between 6% and 9%. RFA is currently performed with all three approaches. There is a compelling need for more research to determine the efficacy and utility of RFA to increase local recurrence-free, progression-free, and disease-free survival as well as OS for patients with hepatic metastases from colorectal cancer (CRHM). Clinical trials have established that hepatic resection can improve OS for patients with resectable CRHM, however additional studies are needed.

Although there is a paucity of clinical RCT data to establish the efficacy and utility of RFA for CRHM, it has been proposed and used at times in the United States and other countries. Two recent RCTs were closed as a result of nonaccrual, and results have not been published; the European Organization for Research and Treatment of Cancer Chemotherapy + Local Ablation Versus Chemotherapy (CLOC+C) Trial and a National Surgical Adjuvant Breast and Bowel Project trial comparing oxaliplatin, capecitabine, and hepatic arterial infusion of floxuridine with oxaliplatin and capecitabine in patients with resected or ablated liver metastases from colorectal cancer.
Multiple factors contribute to the paucity of RCT evidence on outcomes of RFA for CRHM. The reluctance of patients to be randomly assigned may be one factor. Another is that many clinicians are reluctant to enroll patients onto trials because they are convinced that currently available data from highly selected patient series is sufficient evidence and discount patient selection bias and other threats to validity of conclusions based on such data.

Scientific Rationale – Update February 2011
According to the American Association for the Study of Liver Disease (AASLD), percutaneous ablation is the best treatment option for patients with early stage hepatocellular carcinoma (HCC) who are not suitable for resection or transplantation. The AASLD states, currently, radiofrequency ablation should be the first choice for local ablation, but ethanol injection remains an important therapeutic tool. According to the AASLD guidelines, "Alcohol injection and radiofrequency are equally effective for tumors <2 cm. However, the necrotic effect of radiofrequency ablation is more predictable in all tumor sizes and in addition, its efficacy is clearly superior to that of alcohol injection in larger tumors (level I).”

According to the National Comprehensive Care Network (NCCN), local approaches to the treatment of HCC are directed toward inducing selective tumor necrosis and include two categories, ablation or embolization. They note the effectiveness of these approaches in the treatment of HCC has not been established to be comparable to that of liver resection or transplantation. They note the consensus of the panel is that these methods should not be used for patients who meet surgical selection criteria. The NCCN notes that studies have shown that ablative therapy is most effective on smaller HCC tumors. The consensus of the panel is that ablation therapy alone for the treatment of HCC performs optimally when tumors are ≤ 3cm, and that lesions between 3 and 5 cm may be treated using a combination of ablation and embolization methods. The panel considers percutaneous ablation to be a good option for well-selected patients with small tumors who are not candidates for surgery.

Per the AASLD, local ablation is safe and effective therapy for patients who cannot undergo resection, or as a bridge to transplantation (level II).

Akyildiz et al (2010) reported long-term oncologic results of eighty-nine patients with neuroendocrine hepatic metastases who underwent 119 laparoscopic RFA sessions within 13 years. Data were obtained from a prospective, Institutional Review Board approved database. Univariate Kaplan Meier and multivariate Cox proportional hazards model were used for statistical analyses. Data are expressed as mean ± standard error of the mean. Thirty-five women and 54 men with a mean age of 56 ± 1.4 years were included in this study. Tumor types included were carcinoid (n = 55), pancreatic islet cell (n = 23), and medullary thyroid cancer (n = 11). Mean tumor size was 3.6 ± 0.2 and the number of lesions was 6 ± 1. Perioperative morbidity was 6%, and 30-day mortality was 1%. Symptom relief was achieved in 97% of patients after radiofrequency ablation. Median follow-up was 30 ± 3 months. Twenty-two percent of patients developed local liver recurrence, 63% developed new liver lesions, and 59% developed extrahepatic disease in follow-up. Repeat radiofrequency ablation (27%) and chemoembolization (7%) were used to achieve additional local tumor control in follow up. Median disease-free survival was 1.3 years and the overall survival was 6 years after radiofrequency ablation. Liver tumor volume, symptoms, and extrahepatic disease were independent predictors of survival.
Huang et al (2010) compared the long-term outcomes of surgical resection and RFA for the treatment of small HCC. Two hundred thirty HCC patients who met the Milan criteria and were suitable to be treated by either resection (RES) or RFA entered into a randomized controlled trial. The patients were regularly followed up after treatment for 5 years (except for those who died). The primary end point was overall survival; the secondary end points were recurrence-free survival, overall recurrence, and early-stage recurrence. The 1-, 2-, 3-, 4- and 5-year overall survival rates for the RFA group and the RES group were 86.96%, 76.52%, 69.57%, 66.09%, 54.78% and 98.26%, 96.52%, 92.17%, 82.60%, 75.65%, respectively. The corresponding recurrence-free survival rates for the 2 groups were 81.74%, 59.13%, 46.08%, 33.91%, 28.69% and 85.22%, 73.92%, 60.87%, 54.78%, 51.30%, respectively. Overall survival and recurrence-free survival were significantly lower in the RFA group than in the RES group. The 1-, 2-, 3-, 4-, and 5-year overall recurrence rates were 16.52%, 38.26%, 49.57%, 59.13%, and 63.48% for the RFA group and 12.17%, 22.60%, 33.91%, 39.13%, and 41.74% for the RES group. The overall recurrence was higher in the RFA group than in the RES group. The investigators concluded surgical resection may provide better survival and lower recurrence rates than RFA for patients with HCC to the Milan criteria.

Many potential candidates with HCC awaiting liver transplant either die before an organ becomes available or drop out from the transplant waiting list because of tumor progression. Bridging therapies such as ablative therapies or transarterial chemoembolization (TACE) have been investigated with the goal to slow down tumor progression and avoid tumor cell dissemination during recipient hepatectomy to decrease the risk of postoperative recurrence. However, the impact of RFA as a bridge to transplantation on the overall survival in HCC patients is still not clearly defined. According to the National Comprehensive Care Network (NCCN), “Studies have investigated the role of locoregional treatment of HCC as bridge to liver transplant in patients on the waiting list for such a procedure. These studies include the use of RFA, chemoembolization, and sorafenib as bridge therapies. However, the small size of these studies and the heterogeneous nature of the study populations as well as the absence of RCT’s evaluating the utility of bridge therapy for reducing the liver transplant waiting list drop out wait, limit the conclusions that can be drawn. Nevertheless, use of bridge therapy in this setting is increasing, and is administered in some NCCN centers.”

Dubay et al (2011) measured the effect of RFA on time to drop-off in HCC-listed patients. Patients with Milan criteria tumors were stratified into RFA (n= 77) and no treatment groups (n= 93). The primary effectiveness of RFA was 83% (complete radiographic response). RFA was associated with a longer median wait time to transplant (9.5 vs. 5 months). Tumor-specific drop-off events were equivalent between RFA (21%) and no treatment (12%) groups. Controlling for wait time, there was no difference in overall (P= 0.56) or tumor-specific drop-off. The investigators reported there were no differences in 5-year overall or tumor-free survivals from list date or transplant. Using multivariate analysis, the likelihood of receiving a transplant and patient survivals were associated with tumor characteristics (AFP, tumor number and size) and not with bridge therapy or waiting time. The investigators concluded RFA allows patients to be maintained longer on the waiting list without negative consequences on drop-off or survival compared with no treatment. Post-transplant outcomes are affected more by tumor characteristics than RFA or wait time.
Heckman et al (2008) sought to examine locoregional therapies and their effect on survival compared with transplantation alone in a retrospective review of a prospectively collected database. 123 patients were included. Patients were analyzed in two groups. Group I consisted of 50 patients that received therapy (20 transcatheter arterial chemoembolization (TACE); 16 yttrium-90 (90)Y; 13 RFA, 3 resections). Group II consisted of 73 patients transplanted without therapy. Median list time was 28 days (range 2-260 days) in group I, and 24 days (range 1-380 days) in group II. Median time from therapy to orthotopic liver transplantation (OLT) was 3.8 months (range 9 days to 68 months). Twelve patients (24%) were successfully downstaged (8 TACE, 2 (90)Y, 2 RFA/resection). Overall 1-, 3-, and 5-year survival were 81%, 74%, and 74%, respectively. Survival was not statistically significantly different between the two groups. The 12 patients downstaged did not have a significant difference in survival as compared with the patients who received therapy but did not respond or the patients who were transplanted without therapy. The investigators concluded this report addressed locoregional therapy for hepatocellular carcinoma as a bridge to transplant. There was no statistical difference in overall survival between patients treated and those not treated prior to transplant. They concluded this provides evidence that locoregional therapy is a safe tool for patients on the transplant list, does not impact survival, and can downstage selected patients to allow life-saving liver transplantation.

In a retrospective study, Vivanco et al (2010) reviewed their experience in relation to bridge therapy prior to orthotopic liver transplantation (OLT) for HCC. Among 29 patients, including 12 who were diagnosed by the explant and 17 prior to transplantation, 88% underwent bridge therapy during a mean waiting time to OLT of 12 months. Among the 23 procedures, namely 1.5 procedures per patient, included most frequently chemoembolization (48%), alcohol ablation (30%), radiofrequency ablation (13%), and surgery (9%). Thirty-three percent of the explants contained lesions within the Milan criteria. In the series the 5-year survival rate for patients transplanted for HCC was 86%; in the bridge therapy group, it was 73%. The reviewers concluded the incidence of patients who underwent bridge therapy (52%) was similar to other reported experiences, but the fulfillment of Milan criteria in the explants was lower. Among the bridge therapy group, the survival was slightly lower, probably because this group displayed more advanced disease.

At the present time, insufficient evidence exists to determine if RFA improves transplantation rates and posttransplantation outcomes.

**Scientific Rationale – Update January 2010**

The incidence of hepatocellular carcinoma (HCC) is increasing in the U.S., chiefly due to increased prevalence of hepatitis C infection. This disease is usually asymptomatic until later stages, and prognosis is generally very poor. Surgery and transarterial chemoembolization have for many years dominated the local treatment of HCC, however surgical resection is rarely done due to the level of progression.

The introduction of image-guided percutaneous techniques for local tumor ablation changed the treatment of liver cancer. Percutaneous techniques of local tumor ablation may be categorized into three major groups: (A) injectables (ethanol, acetic acid, hot saline); (B) heating (radiofrequency, interstitial laser therapy, microwave coagulation therapy and high-intensity focused US); and (C) freezing (cryotherapy). Of these the most widely used are percutaneous ethanol injection and thermal ablation methods.
Percutaneous ethanol injection (PEI) and radiofrequency ablation (RFA) have both successfully been employed in the treatment of HCC. In current guidelines both techniques are recommended as standard therapy in limited liver cancer. From the current literature both techniques have to be considered safe and effective in the treatment of HCC.

PEI of liver tumors is a technique in which pure alcohol is injected into liver cancers to kill the cancer cells. The alcohol is injected through the skin into the tumor using a very thin needle with the help of ultrasound or CT visual guidance. Alcohol induces tumor destruction by drawing water out of tumor cells (dehydrating them) and thereby altering (denaturing) the structure of cellular proteins. It may take up to five or six sessions of injections to completely destroy the cancer.

Per the National Cancer Comprehensive Network (NCCN) Practice Guidelines of Oncology on Hepatobiliary Cancer (2010):

‘Induction of tumor necrosis can be achieved by direct exposure of the tumor to a particular chemical substance (et. ethanol or acetic acid) or an alteration in temperature (Radiofrequency ablation (RFA), microwave ablation or cryotherapy). Any ablative therapy can be performed by laparoscopic, percutaneous or open approaches. The most commonly used methods of ablation are RFA or percutaneous ethanol injection (PEI) therapy. Selection criteria include patients with local disease only characterized by as being completely amenable to ablative therapy according to the size and location of the tumor. The complication rate associated with ablative therapy in the treatment of HCC has been reported to be relatively low. For example in a randomized controlled trial by Lin et al. (2005), the treatment of patients with HCC using RFA were compared with percutaneous ethanol injection (PEI), and the major complications or mortality rates were 4.8% and 0% respectively.’

(2008) The National Cancer Institute (NCI) states that, along with RFA, chemoembolization and cryosurgery, PEI is a standard treatment option for small (< 5 cm), localized, unresectable tumors in patients with primary liver cancer.

The ideal patient for alcohol injection has fewer than three Hepatocellular Carcinoma (HCC) tumors, each of which is:

- Well defined (distinct margins)
- Less than 5cm in diameter or several small tumors measuring 3-4 cm in diameter
- Surrounded by a shell consisting of scar tissue (fibrous encapsulation)
- Not near the surface of the liver

Patients are typically not candidates for percutaneous ethanol injection if they have evidence of extrahepatic metastases. In addition, patients with HCC undergoing alcohol injection should have no signs of chronic liver failure, such as ascites or jaundice. (Patients with liver failure would not be able to tolerate the alcohol injections.) By injecting pure alcohol (i.e., ethanol) through the skin via ultrasonic or computerized tomographic (CT) guidance into the tumor bed, blood flow to the cancer is blocked. The alcohol induces tumor destruction by drawing water out of the tumor cells (dehydrating them) and denaturing the structure of the cellular proteins. It may take several injections to completely destroy the tumor. This procedure can be done under local anesthetic and on an outpatient basis. Due to the relation of PEI
effectiveness to tumor size, PEI therapy is generally appropriate only in those patients with fewer than four lesions, each less than 3–4 cm in size or with a small single lesion less than 5 cm. PEI is most frequently used for treatment of primary HCC, because the multifocal nature of the disease and the common association with cirrhosis often make resection of even small amounts of liver prohibitively high risk (Cancer Medicine, 2003)

The most common side effect of alcohol injection is leakage of alcohol onto the surface of the liver and into the abdominal cavity, thereby causing pain and fever. It is important that the location of the tumor relative to the adjacent blood vessels and bile ducts is clearly identified. The reason for needing to locate these structures is to avoid injuring them during the procedure and causing bleeding, bile duct inflammation, or bile leakage.

Evidence in the published, peer-reviewed scientific literature supports the use of PEI for the treatment of small HCC. A randomized, controlled three-armed study of 157 patients with HCC conducted by Lin et al. (2004) compared the clinical outcomes of RFA, conventional PEI and higher-dose PEI. The rate of complete tumor necrosis for patients receiving conventional PEI was 88%; local tumor progression at one, two and three years for the PEI group was 23%, 45% and 45%, respectively. The overall survival rates for the PEI groups at one, two and three years were 85%, 61%, and 50% in the conventional PEI group and 88%, 63% and 55% in the higher-dose PEI group, respectively. Cancer-free survival for the PEI groups was 61%, 42% and 17% for the conventional dose group; 63%, 45%, and 20% for the higher-dose PEI group; and 78%, 59% and 37% for the RFA group. Study results suggest that PEI delivered conventionally (single injection) or at a higher dose (multiple sites, simultaneous injections) is equivalent to RFA in the treatment of patients with lesions measuring 3–5 cm in diameter.

Per the European Journal of Ultrasound, (2001), percutaneous ethanol injection therapy (PEI) has been widely practiced in the treatment of liver tumors, especially of hepatocellular carcinoma (HCC). Histopathologic examinations, findings in imaging modalities and serum tumor marker levels have shown a remarkable anticancer effect of this procedure. In addition, PEI has achieved considerably high long-term survival rates.

**Scientific Rationale – Initial**

Hepatocellular carcinoma (HCC), also referred to as malignant hepatoma, is an aggressive hepatic neoplasm that most commonly affects adults and accounts for 80% to 90% of all liver cancers. It occurs more often in men than women and occurs mostly in people 50 to 60 years old. HCC is relatively uncommon in the United States, being more common in parts of Africa and Asia. The cause of liver cancer is unknown, but major contributing factors include chronic liver disease with cirrhosis, viral hepatitis and hemochromatosis. Hepatitis B infection and hepatitis C infection appear to be the most significant causes of hepatocellular carcinoma worldwide. HCC is associated with cirrhosis in 50% to 80% of patients; 5% of cirrhotic patients eventually develop hepatocellular cancer, which is often multifocal. The primary signs of hepatocellular carcinoma are those of a hepatic mass. Among patients with underlying cirrhotic disease, a progressive increase in alpha-fetoprotein (AFP) and/or in alkaline phosphatase or a rapid deterioration of hepatic function may be the only clue to the presence of the neoplasm.
Although complete surgical resection remains the gold-standard in the treatment of liver tumors, a large number of patients have disease that is not amenable to surgical therapy. This may be due to tumor size, location near major intrahepatic blood vessels precluding a margin-negative resection, multifocality, or inadequate hepatic function related to coexistent cirrhosis. Any local therapy for malignant hepatic tumors, be it surgical resection, RFA, or some other tumor ablative technique, is generally performed with curative intent, but a significant proportion of patients will subsequently develop clinically detectable hepatic or extrahepatic recurrence from their coexistent micrometastatic disease. Consequently, several treatment modalities have been developed for local control of liver tumors. Complete surgical resection of the tumor with a margin of normal liver is the treatment of choice, but is to only a small fraction of patients (10% to 20%) with localized disease. If the cancer cannot be completely removed, prognosis depends on the degree of local tumor replacement and the extent of liver function impairment. Patients with locally unresectable fibrolamellar variant hepatomas may be considered for liver transplantation. Aggressive surgery or liver transplantation may be successful in treating small or slow-growing tumors if they are diagnosed early, but the limited availability of livers for transplantation restricts the use of this approach.

Colorectal carcinoma remains a serious clinical problem despite recently intensified screening. In 2001, an estimated 135,400 new cases were anticipated with 56,700 deaths in the United States. The majority of deaths associated with colorectal cancer are due, at least in part, to liver metastases, the most common site of distant metastasis. About one-fourth of patients with liver metastases from colorectal cancer have no other sites of metastasis and can be treated with regional therapies directed toward their liver tumors. Based on a preponderance of uncontrolled studies for hepatic metastatic colorectal carcinoma, the gold standard of surgical resection offers the only potential for cure of selected patients with completely resected disease, with 5-year survival rates of only 20-40%; however, due to tumor size, unresectable location, multifocality, inadequate functional hepatic reserve or presence of extrahepatic disease, it is estimated that as much as 80% of liver tumors are not amenable to surgery at the time of diagnosis and, historically, have a 0% five-year survival.

Thus, the treatment options for malignant liver tumors are limited for the majority of patients. Whether primary or metastatic, whether initial or recurrent, alternative treatment approaches to control and potentially cure the liver tumors have been investigated. Studies show that long-term survivors are rare with systemic chemotherapy, and external beam radiation is associated with a high complication rate. Infusional chemotherapy through the hepatic artery involves the surgical implantation of a port and the infusion of one or more chemotherapeutic drugs into the liver. Alternatively, ablative techniques treat malignant nodules by direct destruction with either thermal or chemical methods, including percutaneous ethanol injection (PEI), radiofrequency ablation and cryotherapy.

In 2000, the FDA approved the use of radiofrequency ablation (RFA), also known as radiofrequency thermal ablation, (RFTA), for localized primary or metastatic liver tumors. RFA is a technique that works by passing electrical current in the range of radiofrequency waves between. special needle electrodes inserted directly into the center of a tumor and the grounding pads placed on the patient’s skin. The delivery of alternating current causes local thermal destruction by protein denaturation and coagulation necrosis. RFA may be given through a percutaneous route under the guidance of an imaging method such as ultrasound, computed tomography (CT).
scanning or magnetic resonance (MR) imaging. Intraoperative or laparoscopic approaches are also options. The energy level and thus the heating effect dissipates rapidly at an increasing distance from the electrodes so that the highest temperature will always be at the points nearest to the electrodes. The size of the ultimate lesion is determined by the size of the probe. Initial devices created elliptical lesions with a diameter between 2 and 3.5 cm. Recent advances have led to catheter probes up to 7 cm in diameter. The size of the thermal lesion is one of the major limitations of RFA. If there are multiple tumor nodules they may be treated in one or more sessions. Because healthy liver tissue withstands more heat than a tumor, radiofrequency ablation is able to destroy a tumor and a small rim of normal tissue about its edges without affecting most of the normal liver. The dead tumor cells are gradually replaced by scar tissue that shrinks over time. RFA may be repeated as needed should the tumor recur.

The outcomes of radiofrequency ablation have been reported in numerous case series. Although there have been inadequate controlled studies of homogenous groups of patients, the available data suggests that local ablation of primary or metastatic liver cancer can be an alternative to surgery. In most studies, more than half the liver tumors treated by radiofrequency ablation have not recurred. Treatment-related serious complications are infrequent.

**Review History**

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<td>March 16, 2004</td>
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<td>April 2006</td>
<td>Update - no changes</td>
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<td>Update - No revisions. Coding updates.</td>
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<tr>
<td>January 2010</td>
<td>Update. Changed title to 'Ablation of Liver Tumors’. Added percutaneous ethanol injection of liver tumor as medically necessary with specific criteria. Codes reviewed.</td>
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<tr>
<td>February 2011</td>
<td>Update – no revisions</td>
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<td>Update – no revisions</td>
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**This policy is based on the following evidence-based guidelines:**


References – Update February 2016


References – Update February 2015


References – Update February 2014


References – Update February 2013

References – Update September 2012

References – Update October 2011

References – Update February 2011

Radiofrequency Ablation of Liver Tumors Feb 16

References – Update January 2010

Radiofrequency Ablation of Liver Tumors Feb 16

References – Update May 2008

References – Initial
5. Chopra S, Dodd GD, Chanin MP et al. Radiofrequency ablation of hepatic tumors adjacent to the gallbladder: feasibility and safety. AJR 2003;180(3):697-701

Important Notice

General Purpose.
Health Net's National Medical Policies (the "Policies") are developed to assist Health Net in administering plan benefits and determining whether a particular procedure, drug, service or supply is medically necessary. The Policies are based upon a review of the available clinical information including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the drug or device, evidence-based guidelines of governmental bodies, and evidence-based guidelines and positions of select national health professional organizations. Coverage determinations are made on a case-by-case basis and are subject to all of the terms, conditions, limitations, and exclusions of the member's contract, including medical necessity requirements. Health Net may use the Policies to determine whether under the facts and circumstances of a particular case, the proposed procedure, drug, service or supply is medically necessary. The conclusion that a procedure, drug, service or supply is medically necessary does not constitute coverage. The member's contract defines which procedure, drug, service or supply is covered, excluded, limited, or subject to dollar caps. The policy provides for clearly written, reasonable and current criteria that have been approved by Health Net's National Medical Advisory Council (MAC). The clinical criteria and medical policies provide guidelines for determining the medical necessity criteria for specific procedures, equipment, and services. In order to be eligible, all services must be medically necessary and otherwise defined in the member's benefits contract as described this "Important Notice" disclaimer. In all cases, final benefit determinations are based on the applicable contract language. To the extent there are any conflicts between medical policy guidelines and applicable contract language, the contract language prevails. Medical policy is not intended to override the policy that defines the member's benefits, nor is it intended to dictate to providers how to practice medicine.

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The date of posting is not the effective date of the Policy. The Policy is effective as of the date determined by Health Net. All policies are subject to applicable legal and regulatory mandates and requirements for prior notification. If there is a discrepancy between the policy effective date and legal mandates and regulatory requirements, the requirements of law and regulation shall govern. * In some states, prior notice or posting on the website is required before a policy is deemed effective. For information regarding the effective dates of Policies, contact your provider representative. The Policies do not include definitions. All terms are defined by Health Net. For information regarding the definitions of terms used in the Policies, contact your provider representative.

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No Medical Advice.
The Policies do not constitute medical advice. Health Net does not provide or recommend treatment to members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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The Policies do not constitute authorization or guarantee of coverage of particular procedure, drug, service or supply. Members and providers should refer to the Member contract to determine if exclusions, limitations, and dollar caps apply to a particular procedure, drug, service or supply.

Policy Limitation: Member's Contract Controls Coverage Determinations.

Radiofrequency Ablation of Liver Tumors Feb 16
Statutory Notice to Members: The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illnesses or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. The determination of coverage for a particular procedure, drug, service or supply is not based upon the Policies, but rather is subject to the facts of the individual clinical case, terms and conditions of the member’s contract, and requirements of applicable laws and regulations. The contract language contains specific terms and conditions, including pre-existing conditions, limitations, exclusions, benefit maximums, eligibility, and other relevant terms and conditions of coverage. In the event the Member’s contract (also known as the benefit contract, coverage document, or evidence of coverage) conflicts with the Policies, the Member’s contract shall govern. The Policies do not replace or amend the Member’s contract.

**Policy Limitation: Legal and Regulatory Mandates and Requirements**
The determinations of coverage for a particular procedure, drug, service or supply is subject to applicable legal and regulatory mandates and requirements. If there is a discrepancy between the Policies and legal mandates and regulatory requirements, the requirements of law and regulation shall govern.

**Reconstructive Surgery**
CA Health and Safety Code 1367.63 requires health care service plans to cover reconstructive surgery. "Reconstructive surgery" means surgery performed to correct or repair abnormal structures of the body caused by congenital defects, developmental abnormalities, trauma, infection, tumors, or disease to do either of the following:

1. To improve function or
2. To create a normal appearance, to the extent possible.

Reconstructive surgery does not mean "cosmetic surgery," which is surgery performed to alter or reshape normal structures of the body in order to improve appearance.

Requests for reconstructive surgery may be denied, if the proposed procedure offers only a minimal improvement in the appearance of the enrollee, in accordance with the standard of care as practiced by physicians specializing in reconstructive surgery.

**Reconstructive Surgery after Mastectomy**
California Health and Safety Code 1367.6 requires treatment for breast cancer to cover prosthetic devices or reconstructive surgery to restore and achieve symmetry for the patient incident to a mastectomy. Coverage for prosthetic devices and reconstructive surgery shall be subject to the co-payment, or deductible and coinsurance conditions, that are applicable to the mastectomy and all other terms and conditions applicable to other benefits. "Mastectomy" means the removal of all or part of the breast for medically necessary reasons, as determined by a licensed physician and surgeon.

**Policy Limitations: Medicare and Medicaid**
Policies specifically developed to assist Health Net in administering Medicare or Medicaid plan benefits and determining coverage for a particular procedure, drug, service or supply for Medicare or Medicaid members shall not be construed to apply to any other Health Net plans and members. The Policies shall not be interpreted to limit the benefits afforded Medicare and Medicaid members by law and regulation.