04-77260-21

Original Effective Date: 11/15/10

Reviewed: 08/28/25

Revised: 09/15/25

Subject: Selective Internal Radiation Therapy

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions	Related Guidelines
Other	References	Updates			

DESCRIPTION:

Selective internal radiation therapy (SIRT) also referred to as intrahepatic radioembolization is the intra-arterial delivery of small beads (microspheres) impregnated with yttrium-90 via the hepatic artery. SIRT is performed by threading a catheter from the groin into the hepatic artery. Radioactive isotopes containing yttrium-90 are delivered to the liver tumor through a catheter placed into the hepatic artery emitting localized radiation therapy. This therapy is proposed as a treatment for both primary and metastatic liver tumors.

The Food and Drug Administration (FDA) has approved two commercial forms of 90Y microspheres; TheraSphere® (MDS Nordion) and SIR-Spheres® (Sirtex Medical). TheraSphere® are glass microspheres, indicated for radiation treatment or as a neoadjuvant to surgery or transplantation in patients with unresectable hepatocellular carcinoma (HCC) who can have placement of appropriately positioned hepatic arterial catheters. TheraSphere® was approved by the FDA under Humanitarian Device Exemption. SIR-Spheres® are resin microspheres, indicated for the treatment of unresectable metastatic liver tumors from primary colorectal with adjuvant intra-hepatic artery chemotherapy (IHAC) of Floxuridine (FUDR).

Summary and Analysis of Evidence: Gabr et al (2021) reported long-term outcomes of liver transplantation (LT) for patients with hepatocellular carcinoma (HCC) who were bridged/downstaged by Y90. Patients undergoing LT following Y90 between 2004 and 2018 were included, with staging by United Network for Organ Sharing (UNOS) tumor-node-metastasis criteria at baseline pre-Y90 and pre-LT. Post-Y90 toxicities were recorded. Histopathological data of HCC at explant were recorded. Long-term outcomes, including overall survival (OS), recurrence-free survival (RFS), disease-specific mortality (DSM), and time-to-recurrence, were reported. Time-to-endpoint analyses were estimated using Kaplan-

Meier. Univariate and multivariate analyses were performed using a log-rank test and Cox proportional-hazards model, respectively. During the 15-year period, 207 patients underwent LT after Y90. OS from LT was 12.5 years, with a median time to LT of 7.5 months [interquartile range, 4.4-10.3]. A total of 169 patients were bridged, whereas 38 were downstaged to LT. Respectively, 94 (45%), 60 (29%), and 53 (26%) patients showed complete, extensive, and partial tumor necrosis on histopathology. Three-year, 5-year, and 10-year OS rates were 84%, 77%, and 60%, respectively. Twenty-four patients developed recurrence, with a median RFS of 120 (95% confidence interval, 69-150) months. DSM at 3, 5, and 10 years was 6%, 11%, and 16%, respectively. There were no differences in OS/RFS for patients who were bridged or downstaged. RFS was higher in patients with complete/extensive versus partial tumor necrosis ($P < 0.0001$). For patients with UNOS T2 treated during the study period, 5.2% dropped out because of disease progression. The authors conclude that Y90 is an effective treatment for HCC in the setting of bridging/downstaging to LT. Patients who achieved extensive or complete necrosis had better RFS, supporting the practice of neoadjuvant treatment before LT.

Liu et al (2022) conducted a meta-analysis to assess the efficacy of yttrium-90 selective internal radiation therapy (SIRT) in treating patients with breast cancer with hepatic metastasis. A total of 24 studies from 14 institutions were included in the present meta-analysis. On the basis of the data from 412 patients, post-embolization MST was 9.8 [95% confidence interval (CI): 9.0-11.6] months. Patients with additional extrahepatic metastasis had a poorer survival rate compared with those with localized hepatic metastasis only (MST: 5.3 vs. 15 months, $p < 0.0001$). Patients with <25% liver tumor burden exhibited more promising survival than those with >25% (MST: 10.5 vs. 6.8 months, $p < 0.0139$). On the basis of RECIST, mRECIST, and PERCIST criteria, tumor response rate was 36% (95% CI: 26%-47%), 49% (95% CI: 34%-65%), and 47% (95% CI: 17%-78%), respectively, whereas tumor control rate was 85% (95% CI: 76%-93%), 73% (95% CI: 59%-85%), and 97% (95% CI: 91%-100%), respectively. The authors concluded that SIRT is feasible and effective in treating patients with breast cancer with liver metastasis. Patients with lower hepatic tumor burden and without extrahepatic metastasis demonstrated more survival benefit. Future randomized controlled trials are warranted.

Gonsalves et al (2011) assessed the safety and efficacy of radioembolization in the management of hepatic metastasis of uveal melanoma after failure of immunoembolization or chemoembolization. From January 2007 through April 2009, 32 patients underwent radioembolization therapy for hepatic metastasis of uveal melanoma. Pretreatment tumor burdens were divided into three categories: less than 25% (n = 25), 25-50% (n = 5), and greater than 50% (n = 2). Toxicity, extrahepatic disease, and hepatic tumor response were assessed 1 month and then every 3 months after treatment. Best radiographic response of hepatic metastasis was determined with the Response Evaluation Criteria in Solid Tumors criteria. Overall survival and progression-free survival of hepatic metastasis were estimated by Kaplan-Meier analysis. Differences in survival between subgroups were evaluated by log-rank test in univariate analysis. The clinical follow-up period ranged from 1.0 to 29.0 months (median, 10.0 months). The median overall survival was 10.0 months, and the progression-free survival of hepatic metastasis, 4.7 months. Twenty-two patients died 1.0-29.0 months (median, 5.8 months) after treatment owing to progression of liver disease (n = 13), extrahepatic disease (n = 4), or both (n = 5). Patients who had a pretreatment tumor burden less than 25% had longer median overall survival (10.5 vs 3.9 months, $p = 0.0003$) and progression-free survival (6.4 vs 3.0 months, $p = 0.03$) than patients who had a pretreatment tumor burden of 25% or greater. Patients who had a complete response (n = 1), partial response (n = 1), or stable disease (n = 18) had longer median overall survival (14.7 vs 4.9 months, $p = 0.0006$) and progression-free survival of hepatic metastasis (7.9 vs 3.1 months, $p < 0.0001$) than patients with tumor progression (n = 12). Self-limiting grade 1-2 systemic toxicity included tiredness (n = 9), indigestion (n = 2), and abdominal discomfort (n = 5). Grade 3-4 hepatic toxicity was attributed to tumor progression. The authors concluded that radioembolization is safe and effective salvage therapy for limited metastasis of uveal melanoma.

Devicie et al (2014) evaluate the efficacy of (90)Y resin radioembolization is an emerging treatment in patients with liver-dominant metastatic neuroendocrine tumors (mNETs). One hundred fifty-six studies were screened; 12 were selected, totaling 435 procedures for response assessment. Funnel plots showed no evidence of publication bias (P = 0.841). Critical appraisal revealed a median of 75% of desired criteria included in selected studies. Very high between-study heterogeneity ruled out a fixed-effects model. The random-effects weighted average objective response rate (complete and partial responses, CR and PR, respectively) was 50% (95% confidence interval, 38%-62%), and weighted average disease control rate (CR, PR, and stable disease) was 86% (95% confidence interval, 78%-92%). The percentage of patients with pancreatic mNET was marginally associated with poorer response (P = 0.030), accounting for approximately 23% of the heterogeneity among studies. The percentage of CR and PR correlated with median survival (R = 0.85; P = 0.008). The authors concluded that meta-analysis confirms radioembolization to be an effective treatment option for patients with hepatic mNET. The pooled data demonstrated a high response rate and improved survival for patients responding to therapy.

POSITION STATEMENT:

Selective internal radiation therapy (SIRT) with an FDA approved microsphere **meets the definition of medical necessity** for the following:

- Unresectable metastatic liver tumors from primary colorectal cancer (CRC); **OR**
- Unresectable primary hepatocellular carcinoma (HCC); **OR**
- In primary hepatocellular carcinoma as a bridge to liver transplantation; **OR**
- To treat hepatic metastases from neuroendocrine tumors (carcinoid and noncarcinoid) with diffuse and symptomatic disease when systemic therapy (e.g., chemotherapy) has failed to control symptoms**; OR**
- To treat primary intrahepatic cholangiocarcinoma in members with unresectable tumors**; OR**
- To treat unresectable hepatic metastases from liver predominant melanoma (ocular or cutaneous) that is both progressive and diffuse, in members who are refractory to chemotherapy or are not candidates for chemotherapy or other systemic therapies**; OR**
- To treat unresectable hepatic metastases from liver predominant breast cancer that is both progressive and diffuse, in members who are refractory to chemotherapy or are not candidates for chemotherapy or other systemic therapies.

Selective internal radiation therapy is considered **experimental or investigational** for all other indications, due to insufficient evidence to support conclusions regarding the effect of selective internal radiation therapy on health outcomes.

BILLING/CODING INFORMATION:

HCPCS Code:

S2095	Transcatheter occlusion or embolization for tumor destruction, percutaneous, any method, using yttrium-90 microspheres

ICD-10 Diagnosis Codes That Support Medical Necessity:

C18.0 – C18.9	Malignant neoplasm of colon
C22.0	Liver cell carcinoma

C22.2	Hepatoblastoma
C22.3	Angiosarcoma of liver
C22.4	Other sarcomas of liver
C22.7	Other specified carcinomas of liver
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C7B.02	Secondary carcinoid tumors of liver
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct

LOINC Codes:

The following information may be required documentation to support medical necessity: physician history and physical, physician progress notes, plan of treatment and reason for selective internal radiation therapy.

Documentation Table	LOINC Codes	LOINC Time Frame Modifier Code	LOINC Time Frame Modifier Codes Narrative
Physician history and physical	28626-0	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim
Attending physician progress note	18741-9	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim
Plan of treatment	18776-5	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Humanitarian Device Exemption (HDE) a Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year. An approved HDE authorizes marketing of the HUD. An HUD may only be used in facilities that have established a local institutional review board (IRB) to supervise clinical testing of the HUD and after the IRB has approved the use of the device to treat or diagnose the specific disease (FDA , 2010).

RELATED GUIDELINES:

Brachytherapy-Oncologic Applications, 04-777260-20

OTHER:

Other names used to report selective internal radiation therapy:

Intra-arterial brachytherapy
Radioembolization (RE)
Selective Internal Radiation (SIRT)
Transarterial embolization (TARE)

REFERENCES:

1. ACR–ABS–ACNM–ASTRO–SIR–SNMMI Practice Parameter for Radioembolization of Liver Malignancies, 2024.
2. ACR-SIR Practice Guideline for Radioembolization with Microsphere Brachytherapy Device (RMBD) for Treatment of Liver Malignancies, 2014.
3. Ahmed O, Yu Q, Patel M, et al. Yttrium-90 Radioembolization and Concomitant Systemic Gemcitabine, Cisplatin, and Capecitabine as the First-Line Therapy for Locally Advanced Intrahepatic Cholangiocarcinoma. J Vasc Interv Radiol. 2023 Apr;34(4):702-709. [Abstract]
4. Al-Adra DP, Gill RS, Axford SJ et al. Treatment of unresectable intrahepatic cholangiocarcinoma with yttrium-90 radioembolization: a systematic review and pooled analysis. European Journal of surgical Oncology 2015; 41(1):120-7.
5. American College of Radiology (ACR) Appropriateness Criteria® Radiologic Management of Hepatic Malignancy, 2015.
6. Atassi B, Bangash AK, Bahrani A et al. Multimodality imaging following 90Y radioembolization: a comprehensive review and pictorial essay. Radiographics 2008; 28(1): 81-99.
7. Bangash AK, Atassi B, Kaklamani V et al. 90 Y radioembolization of metastatic breast cancer to the liver: toxicity, imaging response, survival. Journal of Vascular Interventional Radiology 2007; 18(5):621-628.
8. Blue Cross Blue Shield Association Medical Policy Reference Manual Radioembolization for Primary and Metastatic Tumors of the Liver 8.01.43, 8/24.

9. Cao CQ, Yan TD, Bester L et al. Radioembolization with yttrium microspheres for neuroendocrine tumour liver metastases. British Journal of Surgery 2010; 97(4): 537-543.
10. Chan SL, Chotipanich C, Choo SP, et al. Selective Internal Radiation Therapy with Yttrium-90 Resin Microspheres Followed by Gemcitabine plus Cisplatin for Unresectable Intrahepatic Cholangiocarcinoma: A Phase 2 Single-Arm Multicenter Clinical Trial. Liver Cancer. 2022 Jun 15;11(5):451-459.
11. Coldwell DM, Kennedy AS, Nutting CW. Use of yttrium-90 microspheres in the treatment of unresectable hepatic metastases from breast cancer. International Journal of Radiation Oncology, Biology, Physics 2007; 69(3): 800-804.
12. Coldwell D, Kennedy A, Sangro et al. Integrating radioembolisation into current treatment options for liver tumors: an international working group report. American Journal of Clinical Oncology 2012; 35(1): 81-90.
13. Dancey JE, Shepard FA, Paul K et al. Treatment of nonresectable hepatocellular carcinoma with intrahepatic 90Y-microspheres. Journal of Nuclear Medicine 2000; 41(10): 1673-1681.
14. Devicic Z, Rosenberg J, Braat AJ et al. The efficacy of hepatic 90Y resin radioembolization for metastatic neuroendocrine tumors: a meta-analysis. Journal of Nuclear Medicine 2014; 55(9): 1404-1410.
15. Duke E, Deng J, Ibrahim SM et al. Agreement between competing imaging measures of response of hepatocellular carcinoma to yttrium-90 radioembolization. Journal of Vascular Interventional Radiology 2010; 21(4): 515-512.
16. Egger ME, Armstrong E, Martin RC 2nd, et al. Chemoembolization vs radioembolization for Nenuroendocrine liver metastases: A multi-institutional analysis. J Am Coll Surg. 2020 Apr;230(4):363-370. [Abstract]
17. Engelman ES, Leon-Ferre R, Naraev BG et al. Comparison of transarterial liver-directed therapies for low-grade metastatic neuroendocrine tumors in a single institution. Pancreas 2014; 43(2): 219-25.
18. Facciorusso A, Bargellini I, Cela M, et al. Comparison between Y90 radioembolization plus Sorafenib and Y90 radioembolization alone in the treatment of hepatocellular carcinoma: A propensity score analysis. cancers (Basel). 2020 Apr 7;12(4):897.
19. Frilling A, Clift AK, Braat AJAT, et al. Radioembolisation with 90Y microspheres for neuroendocrine liver metastases: an institutional case series, systematic review and meta-analysis. HPB (Oxford). 2019 Jul;21(7):773-783. [Abstract]
20. Gabr A, Kulik L, Mouli S, et al. Liver transplantation following Yttrium-90 radioembolization: 15-year experience in 207-patient cohort. Hepatology. 2021 Mar;73(3):998-1010. [Abstract]
21. Gonsalves CF, Eschelman DJ, Adamo RD, et al. A prospective phase II trial of radioembolization for treatment of uveal melanoma hepatic metastasis. Radiology 2019 Oct;293(1): 223-231.
22. Gonsalves CF, Eschelman DJ, Sullivan KL et al. Radioembolization as Salvage therapy for hepatic metastasis of uveal melanoma: a single-institution experience. Vascular and Interventional radiology 2011; 196(2): 468-473.
23. Gray B, Van Hazel G, Hope M et al. Randomised trial of SIR-Spheres plus chemotherapy vs. chemotherapy alone for treating patients with liver metastases from primary large bowel cancer. Annals of Oncology 2001; 12(12): 1711-1720.

24. Herba MJ, Thirlwell MP. Radioembolization for hepatic metastases. Seminars in Oncology 2002; 29(2): 152-159.

25. Hendlisz A, Van den Eynde M, Peeters M et al. Phase III trial comparing protracted intravenous fluorouracil infusion alone or with yttrium-90 resin microspheres radioembolization for liver-limited metastatic colorectal cancer refractory to standard chemotherapy. Journal of Clinical Oncology 2010; 28(32): 3687-3694.

26. Hoffmann RT, Jakobs TF, Kubisch CH et al. Radiofrequency ablation after selective internal radiation therapy with Yttrium90 microspheres in metastatic liver disease-is it feasible? European Journal of Radiology 2010; 94(1): 199-205.

27. Ibrahim SM, Lewandowski RJ, Sato KT et al. Radioembolization for the treatment of unresectable hepatocellular carcinoma: a clinical review. Worl Journal of Gastroenterology 2008; 14(11): 1664-1669.

28. Ibrahim SM, Mulcahy MF, Lewandowski RJ et al. Treatment of unresectable cholangiocarcinoma using yttrium-90 microspheres: results from a pilot study. Cancer 2008; 113(8): 2119-2128.

29. Jakobs TF, Hoffmann RT, Fischer T et al. Radioembolization in patients with hepatic metastases from breast cancer. Journal of Vascular and interventional Radiology 2008; 19(5): 683-690.

30. Jia Z, Paz-Fumagalli R, Frey G et al. Resin-based Yttrium-90 microspheres for unresectable and failed first-line chemotherapy intrahepatic cholangiocarcinoma: preliminary results. Journal of Cancer Research and Clinical Research 2017; 143(3): 481-489.

31. Kennedy AS, Dezarn WA, McNeillie P et al. Radioembolization for unresectable neuroendocrine hepatic metastases using resin 90Y-microspheres: early results in 148 patients. American Journal of Clinical Oncology 2008; 31(3):271-279.

32. Kennedy A, Nag S, Salem R et al. Recommendations for radioembolization of hepatic malignancies using yttrium-90 microsphere brachytherapy: a consensus panel report from the radioembolization brachytherapy oncology consortium. International Journal of Radiation Oncology, Biology, Physics 2007; 68(1): 13-23.

33. Kennedy AS, Salem R. Radioembolization (yttrium-90 microspheres) for primary and metastatic hepatic malignancies. Cancer Journal 2010; 16(2): 163-175.

34. King J, Quinn R, Glenn DM et al. Radioembolization with selective internal radiation microspheres for neuroendocrine liver metastases. Cancer 2008; 113(5): 921-929.

35. Kis B, Shridhar R, Mhaskar R, et al. Radioembolization with Yttrium-90 Glass Microspheres as a First-Line Treatment for Unresectable Intrahepatic Cholangiocarcinoma-A Prospective Feasibility Study. J Vasc Interv Radiol. 2023 May 18: S1051-0443(23)00371-8. [Abstract]

36. Kulik LM, Carr BI, Mulcahy MF et al. Safety and efficacy of 90Y radiotherapy for hepatocellular carcinoma with and without portal vein thrombosis. Hepatology 2008; 47(1): 71-81.

37. Kulik L, Heimbach JK, Zaiem F et al. Therapies for patients with hepatocellular carcinoma awaiting liver transplantation: A systematic review and meta-analysis. Hepatology 2018; 67(1): 381-400.

38. Lewandowski RJ, Kulik LM, Riaz A et al. A comparative analysis of transarterial downstaging for hepatocellular carcinoma: chemoembolization versus radioembolization. American Journal of Transplantation 2009; 9(8): 1920-1928.

39. Lim L, Gibbs P, Yip D et al. Prospective study of treatment with selective internal radiation therapy spheres in patients with unresectable primary or secondary hepatic malignancies. Internal Medicine Journal 2005; 35(4); 222-227.

40. Liu C, Tadros G, Smith Q, et al. Selective internal radiation therapy of metastatic breast cancer to the liver: A meta-analysis. Front Oncol. 2022 Nov 24;12: 887653.

41. Mokkarala M, Noda C, Malone C, et al. Comparison of response and outcomes of drug-eluting bead chemoembolization (DEB-TACE) versus radioembolization (TARE) for patients with colorectal cancer liver metastases. Anticancer Res 2019 Jun;39(6):3071-3077 [Abstract]

42. Morris VK, Kennedy EB, Baxter NN, et al. Treatment of Metastatic Colorectal Cancer: ASCO Guideline. J Clin Oncol. 2023 Jan 20;41(3):678-700.

43. Mulcahy MF, Lewandowski RJ, Ibrahim SM et al. Radioembolization of colorectal hepatic metastases using yttrium-90 microspheres. Cancer 2009; 115(8): 1849-1858.

44. Murthy R, Kamat P, Nunez R et al. Radioembolization of yttrium-90 microspheres for hepatic malignancy. Seminars in Interventional Radiology 2008; 25(1): 48-57.

45. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Hepatobiliary Cancers. Version 3.2021-June 15, 2021.

46. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Neuroendocrine and Adrenal Tumors. Version 2.2021-June 18, 2021.

47. National Institute for Health and Care Excellence (NICE) Selective Internal Radiation Therapy for Primary Hepatocellular Carcinoma (IPG460), July 2013.

48. Oladeru OT, Miccio JA, Yang J, et al. Conformal external beam radiation or selective internal radiation therapy-a comparison of treatment outcomes for hepatocellular carcinoma. Journal of Gastrointestinal Oncology 2016; 7(3):433-440.

49. Pitton MB, Kloeckner R, Ruckes C et al. Randomized comparison of selective internal radiotherapy (SIRT) versus drug-eluting bead transarterial chemoembolization (DEB-TACE) for the treatment of hepatocellular carcinoma. Cardiovascular and Interventional Radiology 2015; 38(2): 352-360.

50. Popperl G, Helmberger T, Munzing W et al. Selective internal radiation therapy with SIR-Spheres® in patients with nonresectable liver tumors. Cancer Biotherapy & Radiopharmaceuticals 2005; 20(2): 200-208.

51. Rhee TK, Lewandowski RJ, Liu DM et al. 90Y Radioembolization for metastatic neuroendocrine liver tumors: preliminary results from a multi-institutional experience. Annals of Surgery 2008; 247(6): 1029-1035.

52. Robinson TJ, Du L, Matsuoka L, et al. Survival and Toxicities after Yttrium-90 Transarterial Radioembolization of Cholangiocarcinoma in the RESiN Registry. J Vasc Interv Radiol. 2023 Apr;34(4):694-701.e3. [Abstract]

53. Rowcroft A, Loveday BPT, Thomson BNJ, et al. Systematic review of liver directed therapy for uveal melanoma hepatic metastases. HPB (Oxford). 2020 Apr;22(4):497-505. [Abstract]

54. Rubin D, Nutting C, Jones B. Radioembolization with yttrium microspheres for neuroendocrine tumour liver metastases. British Journal of Surgery 2004; 97(4): 537-543.

55. Salem R, Lewandowski RJ, Mulcahy MF et al. Radioembolization for hepatocellular carcinoma using Yttrium-90 microspheres: a comprehensive report of long-term outcomes. Gastroenterology 2010; 138(1): 52-64.

56. Sato KT, Lewandowski RJ, Mulcahy MF et al. Unresectable chemorefractory liver metastases: radioembolization with 90Y microspheres—safety, efficacy, and survival. Radiology 2008; 247(2): 507-515.

57. Shah RP, Brown KT, Sofocleous CT. Arterially directed therapies for hepatocellular carcinoma. American Journal of Roentgenology 2011; 197(4): W590-W602.

58. Sharma RA, Van Hazel GA Morgan B et al. Radioembolization of liver metastases from colorectal cancer using yttrium-90 microspheres with concomitant systemic oxaliplatin, fluorouracil, and leucovorin chemotherapy. Journal of Clinical Oncology 2007; 25(9): 1099-1106.

59. Society of Interventional Radiology Fact Sheet: Interventional Radiology Treatments for Liver Cancer Minimally Invasive Treatments Help Cancer Patients Extend Life and Improve Quality, 11/04.

60. Stuart, Tan B, Myerson RJ et al. Salvage radioembolization of liver-dominant metastases with a resin-based microsphere: initial outcomes 2008; 19(10): 1427-1433.

61. Stubbs RS, Cannan RJ, Mitchell AW. Selective internal radiation therapy with 90yttrium microspheres for extensive colorectal liver metastases. Journal of Gastrointestinal Surgery 2001; 5(3): 294-302.

62. Stubbs RS, Wickremesekera SK. Selective internal radiation therapy (SIRT): a new modality for treating patients with colorectal liver metastases. Journal of the International Hepto Pancreato Biliary Association 2004; 6(3): 133-139.

63. Tao R, Li X,, Ran R et al. A mixed analysis comparing nine minimally invasive surgeries for unresectable hepatocellular carcinoma patients. Oncotarget 2017; 8(3): 5460-5463.

64. Tice JA. Selective internal radiation therapy or radioembolization for inoperable liver metastases from colorectal cancer. California Technology Assessment Forum. 02/17/10.

65. Townsend A, Price T, Karapetis C. Selective internal radiation therapy for liver metastases from colorectal cancer. Cochrane Database Systematic Reviews 2009 Oct 7; (4): CD007045.

66. van Hazel GA, Heinemann V, Sharma NK, et al. SIRFLOX: Randomized Phase III Trial Comparing First-Line mFOLFOX6 (Plus or Minus Bevacizumab) Versus mFOLFOX6 (Plus or Minus Bevacizumab) Plus Selective Internal Radiation Therapy in Patients With Metastatic Colorectal Cancer. J Clin Oncol. May 20 2016;34(15):1723-1731.

67. Venerito M, Pech M, Canbay A, et al. NEMESIS: Noninferiority, individual-patient metaanalysis of selective internal radiation therapy with 90Y resin microspheres versus Sorafenib in advanced hepatocellular carcinoma. J Nucl Med. 2020 Dec;61(12):1736-1742.

68. Wasan HS, Gibbs P, Sharma NK, et al. FOXFIRE trial investigators; SIRFLOX trial investigators; FOXFIRE-Global trial investigators, van Hazel G, Sharma RA. First-line selective internal radiotherapy plus chemotherapy versus chemotherapy alone in patients with liver metastases from colorectal cancer (FOXFIRE, SIRFLOX, and FOXFIRE-Global): a combined analysis of three multicentre, randomised, phase 3 trials. Lancet Oncol. 2017 Sep;18(9):1159-1171.

69. Yang B, Liang J, Qu Z, et al. Transarterial strategies for the treatment of unresectable hepatocellular carcinoma: A systematic review. PLoS One. 2020 Feb 19;15(2): e0227475.

70. Zori AG, Ismael MN, Limaye AR, et al. Locoregional therapy protocols with and without radioembolization for hepatocellular carcinoma as bridge to liver transplantation. Am J Clin Oncol. 2020 May;43(5):325-333. [Abstract]

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 08/28/25.

GUIDELINE UPDATE INFORMATION:

11/15/10	New Medical Coverage Guideline.
10/01/11	Revision; formatting changes.
12/15/11	Updated position statement; add “In primary hepatocellular carcinoma as a bridge to liver transplantation”, “To treat hepatic metastases from neuroendocrine tumors (carcinoid and noncarcinoid) with diffuse and symptomatic disease when systemic therapy (e.g., chemotherapy) has failed to control symptoms”. Revised experimental or investigational statement; remove “including but not limited to when used as a bridge to transplantation”. Added ICD-9 diagnosis code 209.72 and ICD-10 diagnosis code C7b.02 and C78.7. Updated references.
09/15/12	Scheduled review; position statements maintained and references updated.
05/15/14	Scheduled review; position statements maintained and references updated.
09/15/15	Annual review; added position statement for primary intrahepatic cholangiocarcinoma, unresectable hepatic metastases from liver predominant melanoma (ocular or cutaneous) and unresectable hepatic metastases from liver predominant breast cancer. Added ICD-9 code 197.7. Updated references.
10/01/15	Revision; updated ICD9 and ICD10 coding section.
11/01/15	Revision: ICD-9 Codes deleted.
11/15/16	Revision; no change to position statement. Updated references.
11/15/17	Review; no change to position statement. Updated references.
08/15/19	Review; no change to position statement. Updated references.
09/15/21	Review; no change to position statement. Updated references.
09/15/23	Review; no change to position statement. Updated references.
09/15/24	Review; no change to position statement. Updated references.
09/15/25	Review; no change to position statement. Updated references.