MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

Medical Policy

Radioembolization for Primary and Metastatic Tumors of the Liver

Table of Contents

Policy Number: 292

BCBSA Reference Number: 8.01.43
NCD/LCD: N/A

Related Policies

- Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors, #259
- Cryosurgical Ablation of Primary or Metastatic Liver Tumors, #633
- Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies, #634
- Radiofrequency Ablation of Primary or Metastatic Liver Tumors, #286

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue[SM] and Medicare PPO Blue[SM] Members

Radioembolization may be considered **MEDICALLY NECESSARY** to treat primary hepatocellular carcinoma that is unresectable and limited to the liver.

Radioembolization may be considered **MEDICALLY NECESSARY** in primary hepatocellular carcinoma as a bridge to liver transplantation.

Radioembolization may be considered **MEDICALLY NECESSARY** to treat hepatic metastases from neuroendocrine tumors (carcinoid and noncarcinoid, as classified on pathology report or by WHO classification) with diffuse and symptomatic disease when systemic therapy has failed to control symptoms*.

*Symptomatic disease from metastatic neuroendocrine tumors refers to symptoms related to excess hormone production.

Radioembolization may be considered **MEDICALLY NECESSARY** to treat unresectable hepatic metastases from colorectal carcinoma, melanoma (ocular or cutaneous), or breast cancer that are both progressive and diffuse, in patients with liver-dominant disease who are refractory to chemotherapy or are not candidates for chemotherapy or other systemic therapies.

Radioembolization is considered **INVESTIGATIONAL** for all other hepatic metastases except as noted above.

Radioembolization may be considered **MEDICALLY NECESSARY** to treat primary intrahepatic cholangiocarcinoma in patients with unresectable tumors.

Radioembolization is considered **INVESTIGATIONAL** for all other indications not described above.

Radioembolization should be reserved for patients with adequate functional status (Eastern Cooperative Oncology Group [ECOG] Performance Status 0-2), adequate liver function and reserve, Child-Pugh score A or B, and liver-dominant metastases.

Prior Authorization Information

Inpatient

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

Outpatient

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

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO and Indemnity	Prior authorization is **not required**.
Medicare HMO Blue℠	Prior authorization is **not required**.
Medicare PPO Blue℠	Prior authorization is **not required**.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

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

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

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

HCPCS Codes

HCPCS codes:	Code Description
S2095	Transcatheter occlusion or embolization for tumor destruction, percutaneous, any method, using yttrium-90 microspheres

The following ICD Diagnosis Codes are considered medically necessary when submitted with the HCPCS code above if medical necessity criteria are met:

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
C22.0	Liver cell carcinoma
C22.1	Intrahepatic bile duct carcinoma
C22.2	Hepatoblastoma
C22.3	Angiosarcoma of liver
C22.4	Other sarcomas of liver
C22.7	Other specified carcinomas of liver
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C7B.02	Secondary carcinoid tumors of liver

Description

TREATMENTS FOR HEPATIC AND NEUROENDOCRINE TUMORS

The use of external-beam radiotherapy and the application of more advanced radiotherapy approaches (eg, intensity-modulated radiotherapy) may be of limited use in patients with multiple diffuse lesions due to the low tolerance of normal liver to radiation compared with the higher doses of radiation needed to kill the tumor.

Various nonsurgical ablative techniques have been investigated that seek to cure or palliate unresectable hepatic tumors by improving locoregional control. These techniques rely on extreme temperature changes (cryosurgery or radiofrequency ablation), particle and wave physics (microwave or laser ablation), or arterial embolization therapy including chemoembolization, bland embolization, or radioembolization.

Radioembolization

Radioembolization (referred to as selective internal radiotherapy in older literature) delivers small beads (microspheres) impregnated with yttrium 90 intra-arterially via the hepatic artery. The microspheres, which become permanently embedded, are delivered to tumors preferentially because the hepatic circulation is uniquely organized, whereby tumors greater than 0.5 cm rely on the hepatic artery for blood supply while the normal liver is primarily perfused via the portal vein. Yttrium 90 is a pure beta-emitter with a relatively limited effective range and a short half-life that helps focus the radiation and minimize its spread. Candidates for radioembolization are initially examined by hepatic angiogram to identify and map the hepatic arterial system. At that time, a mixture of technetium 99-labeled albumin particles is delivered via the hepatic artery to simulate microspheres. Single-photon emission computed tomography is used to detect possible shunting of the albumin particles into the gastrointestinal or pulmonary vasculature.

Currently, 2 commercial forms of yttrium-90 microspheres are available: a glass sphere (TheraSphere) and a resin sphere (SIR-Spheres). Noncommercial forms are mostly used outside the United States. While the commercial products use the same radioisotope (yttrium 90) and have the same target dose (100 gray), they differ in microsphere size profile, base material (ie, resin vs glass), and size of commercially available doses. The physical characteristics of the active and inactive ingredients affect the flow of microspheres during injection, their retention at the tumor site, spread outside the therapeutic target region, and dosimetry calculations. The Food and Drug Administration (FDA) granted premarket approval of SIR-Spheres for use in combination with 5-floxuridine chemotherapy by hepatic arterial infusion to treat unresectable hepatic metastases from colorectal cancer. In contrast, TheraSphere's glass sphere was approved under a humanitarian device exemption for use as monotherapy to treat unresectable hepatocellular carcinoma. In 2007, this humanitarian device exemption was expanded to include patients with hepatocellular carcinoma who have partial or branch portal vein thrombosis. For these reasons, results obtained with a product do not necessarily apply to another commercial (or noncommercial) products

Summary

For individuals who have unresectable hepatocellular carcinoma who receive RE or RE with a liver transplant, the evidence includes primarily retrospective and prospective observational studies, with limited evidence from RCTs. Relevant outcomes are overall survival, functional outcomes, quality of life, and treatment-related morbidity. Observational studies have suggested that RE has high response rates compared with historical controls. Two small pilot RCTs have compared RE with alternative therapies for hepatocellular carcinoma, including transarterial chemoembolization and transarterial chemoembolization with drug-eluting beads. Both trials reported similar outcomes for RE compared with alternatives. Evidence from observational studies has demonstrated that RE can permit successful liver transplantation in certain patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have unresectable intrahepatic cholangiocarcinoma who receive RE, the evidence includes case series. Relevant outcomes are overall survival, functional outcomes, quality of life, and treatment-related morbidity. Comparisons of these case series to case series of alternative treatments have suggested that RE for primary intrahepatic cholangiocarcinoma has response rates similar to those seen with standard chemotherapy. RE may play a role for patients with unresectable tumors that are chemorefractory or who are unable to tolerate systemic chemotherapy. However, the evidence is not yet sufficiently robust to draw definitive conclusions about treatment efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have unresectable neuroendocrine tumors who receive RE, the evidence includes an open-label phase 2 study, retrospective reviews, and case series, some of which have compared RE with other transarterial liver-directed therapies. Relevant outcomes are overall survival, functional outcomes, quality of life, and treatment-related morbidity. This evidence has suggested that RE provides outcomes similar to standard therapies and historical controls for patients with neuroendocrine tumor-related symptoms or progression of the liver tumor. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have unresectable intrahepatic metastases from colorectal cancer and prior treatment failure who receive RE, the evidence includes several small- to moderate-sized RCTs, prospective trials, and retrospective studies using a variety of comparators, as well as systematic reviews of these studies. Relevant outcomes are overall survival, functional outcomes, quality of life, and treatment-related morbidity. RCTs of patients with prior treatment failure have methodologic problems, do not show definitive superiority of RE compared with alternatives, but tend to show greater tumor response with RE. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have unresectable intrahepatic metastases from other cancers (eg, breast, melanoma, pancreatic) who receive RE, the evidence includes observational studies. Relevant outcomes are overall survival, functional outcomes, quality of life, and treatment-related morbidity. These studies have shown significant tumor response; however, improvement in survival has not been demonstrated in controlled comparative studies. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

Date	Action
9/2018	BCBSA National medical policy review. No changes to policy statements. New references added. Background and summary clarified.
8/2017	New references added from BCBSA National medical policy.
8/2016	Policy statement on neuroendocrine tumors clarified to indicate carcinoid and noncarcinoid, as classified on pathology report or by WHO classification. 8/1/2016
11/2015	BCBSA National medical policy review. New medically necessary indications described. Clarified coding information. Effective 11/1/2015.

5/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
5/2014	BCBSA National medical policy review. Clarified coding information Investigational indications clarified. Effective 5/1/2014.
1/2014	Coding information clarified.
9/2013	BCBSA National medical policy review. New investigational indications described. Effective 9/1/2013.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
12/1/2011	BCBSA National medical policy review. Changes to policy statements.
4/1/2011	Medical policy 292, effective 04/01/2011, describing covered and non-covered indication.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

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

Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

1. Llovet JM, Real MI, Montana X, et al. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial. *Lancet.* May 18 2002;359(9319):1734-1739. PMID 12049862
2. Lo CM, Ngan H, Tso WK, et al. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. *Hepatology.* May 2002;35(5):1164-1171. PMID 11981766
3. Tao R, Li X, Ran R, et al. A mixed analysis comparing nine minimally invasive surgeries for unresectable hepatocellular carcinoma patients. *Oncotarget.* Jan 17 2017;8(3):5460-5473. PMID 27705924
4. Ludwig JM, Zhang D, Xing M, et al. Meta-analysis: adjusted indirect comparison of drug-eluting bead transarterial chemoembolization versus 90Y-radioembolization for hepatocellular carcinoma. *Eur Radiol.* May 2017;27(5):2031-2041. PMID 27562480
5. Lobo L, Yakoub D, Picado O, et al. Unresectable hepatocellular carcinoma: radioembolization versus chemoembolization: a systematic review and meta-analysis. *Cardiovasc Intervent Radiol.* Nov 2016;39(11):15801588. PMID 27586657
6. Facciorusso A, Serviddio G, Muscatiello N. Transarterial radioembolization vs chemoembolization for hepatocarcinoma patients: A systematic review and meta-analysis. *World J Hepatol.* Jun 28 2016;8(18):770-778. PMID 27366304
7. Vente MA, Wondergem M, van der Tweel I, et al. Yttrium-90 microsphere radioembolization for the treatment of liver malignancies: a structured meta-analysis. *Eur Radiol.* Nov 2009;19(4):951-959. PMID 18989675
8. Kolligs FT, Bilbao JI, Jakobs T, et al. Pilot randomized trial of selective internal radiation therapy vs. chemoembolization in unresectable hepatocellular carcinoma. *Liver Int.* Jun 2015;35(6):1715-1721. PMID 25443863
9. 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. *Cardiovasc Intervent Radiol.* Apr 2015;38(2):352-360. PMID 25373796
10. Padia SA, Johnson GE, Horton KJ, et al. Segmental Yttrium-90 radioembolization versus segmental chemoembolization for localized hepatocellular carcinoma: results of a single-center, retrospective, propensity score-matched study. *J Vasc Interv Radiol.* Jun 2017;28(6):777-785 e771. PMID 28365172
11. Soydal C, Arslan MF, Kucuk ON, et al. Comparison of survival, safety, and efficacy after transarterial chemoembolization and radioembolization of Barcelona Clinic Liver Cancer stage B-C hepatocellular cancer patients. *Nucl Med Commun.* Jun 2016;37(6):646-649. PMID 26905317

12. 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. *J Gastrointest Oncol.* Jun 2016;7(3):433-440. PMID 27284477
13. El Fouly A, Ertle J, El Dorry A, et al. In intermediate stage hepatocellular carcinoma: radioembolization with yttrium 90 or chemoembolization? *Liver Int.* Feb 2015;35(2):627-635. PMID 25040497
14. Gramenzi A, Golfieri R, Mosconi C, et al. Yttrium-90 radioembolization vs sorafenib for intermediate-locally advanced hepatocellular carcinoma: a cohort study with propensity score analysis. *Liver Int.* Mar 2015;35(3):1036-1047. PMID 24750853
15. Carr BI, Kondragunta V, Buch SC, et al. Therapeutic equivalence in survival for hepatic arterial chemoembolization and yttrium 90 microsphere treatments in unresectable hepatocellular carcinoma: a two-cohort study. *Cancer.* Mar 1 2010;116(5):1305-1314. PMID 20066715
16. Kulik L, Heimbach JK, Zaiem F, et al. Therapies for patients with hepatocellular carcinoma awaiting liver transplantation: A systematic review and meta-analysis. *Hepatology.* Jan 2018;67(1):381-400. PMID 28859222
17. Salem R, Gordon AC, Mouli S, et al. Y90 Radioembolization significantly prolongs time to progression compared with chemoembolization in patients with hepatocellular carcinoma. *Gastroenterology.* Dec 2016;151(6):11551163 e1152. PMID 27575820
18. Kulik L, Vouche M, Koppe S, et al. Prospective randomized pilot study of Y90+/-sorafenib as bridge to transplantation in hepatocellular carcinoma. *J Hepatol.* Aug 2014;61(2):309-317. PMID 24681342
19. Tohme S, Sukato D, Chen HW, et al. Yttrium-90 radioembolization as a bridge to liver transplantation: a single-institution experience. *J Vasc Interv Radiol.* Nov 2013;24(11):1632-1638. PMID 24160821
20. Ramanathan R, Sharma A, Lee DD, et al. Multimodality therapy and liver transplantation for hepatocellular carcinoma: a 14-year prospective analysis of outcomes. *Transplantation.* Jul 15 2014;98(1):100-106. PMID 24503764
21. Lewandowski RJ, Kulik LM, Riaz A, et al. A comparative analysis of transarterial downstaging for hepatocellular carcinoma: chemoembolization versus radioembolization. *Am J Transplant.* Aug 2009;9(8):1920-1928. PMID 19552767
22. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Hepatobiliary Cancers. Version 2.2018. https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed June 27, 2018.
23. Al-Adra DP, Gill RS, Axford SJ, et al. Treatment of unresectable intrahepatic cholangiocarcinoma with yttrium-90 radioembolization: A systematic review and pooled analysis. *Eur J Surg Oncol.* Jan 2015;41(1):120-127. PMID 25449754
24. Mouli S, Memon K, Baker T, et al. Yttrium-90 radioembolization for intrahepatic cholangiocarcinoma: safety, response, and survival analysis. *J Vasc Interv Radiol.* Aug 2013;24(8):1227-1234. PMID 23602420
25. Hoffmann RT, Paprottka PM, Schon A, et al. Transarterial hepatic yttrium-90 radioembolization in patients with unresectable intrahepatic cholangiocarcinoma: factors associated with prolonged survival. *Cardiovasc Intervent Radiol.* Feb 2012;35(1):105-116. PMID 21431970
26. Saxena A, Bester L, Chua TC, et al. Yttrium-90 radiotherapy for unresectable intrahepatic cholangiocarcinoma: a preliminary assessment of this novel treatment option. *Ann Surg Oncol.* Feb 2010;17(2):484-491. PMID 19876691
27. Boehm LM, Jayakrishnan TT, Miura JT, et al. Comparative effectiveness of hepatic artery based therapies for unresectable intrahepatic cholangiocarcinoma. *J Surg Oncol.* Feb 2015;111(2):213-220. PMID 25176325
28. Chan LS, Sze DY, Poultsides GA, et al. Yttrium-90 radioembolization for unresectable combined hepatocellular-cholangiocarcinoma. *Cardiovasc Intervent Radiol.* Sep 2017;40(9):1383-1391. PMID 28432387
29. 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. *J Cancer Res Clin Oncol.* Mar 2017;143(3):481-489. PMID 27826686
30. Mosconi C, Gramenzi A, Ascanio S, et al. Yttrium-90 radioembolization for unresectable/recurrent intrahepatic cholangiocarcinoma: a survival, efficacy and safety study. *Br J Cancer.* Jul 26 2016;115(3):297-302. PMID 27336601
31. Rayar M, Sulpice L, Edeline J, et al. Intra-arterial yttrium-90 radioembolization combined with systemic chemotherapy is a promising method for downstaging unresectable huge intrahepatic cholangiocarcinoma to surgical treatment. *Ann Surg Oncol.* Sep 2015;22(9):3102-3108. PMID 25623598

32. Haug AR, Heinemann V, Bruns CJ, et al. 18F-FDG PET independently predicts survival in patients with cholangiocellular carcinoma treated with 90Y microspheres. *Eur J Nucl Med Mol Imaging.* Jun 2011;38(6):10371045. PMID 21308371
33. Ibrahim SM, Mulcahy MF, Lewandowski RJ, et al. Treatment of unresectable cholangiocarcinoma using yttrium-90 microspheres: results from a pilot study. *Cancer.* Oct 15 2008;113(8):2119-2128. PMID 18759346
34. King J, Quinn R, Glenn DM, et al. Radioembolization with selective internal radiation microspheres for neuroendocrine liver metastases. *Cancer.* Sep 1 2008;113(5):921-929. PMID 18618495
35. Devcic Z, Rosenberg J, Braat AJ, et al. The efficacy of hepatic 90Y resin radioembolization for metastatic neuroendocrine tumors: a meta-analysis. *J Nucl Med.* Sep 2014;55(9):1404-1410. PMID 25012459
36. 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.* Mar 2014;43(2):219-225. PMID 24518499
37. Rhee TK, Lewandowski RJ, Liu DM, et al. 90Y Radioembolization for metastatic neuroendocrine liver tumors: preliminary results from a multi-institutional experience. *Ann Surg.* Jun 2008;247(6):1029-1035. PMID 18520231
38. Cao CQ, Yan TD, Bester L, et al. Radioembolization with yttrium microspheres for neuroendocrine tumour liver metastases. *Br J Surg.* Apr 2010;97(4):537-543. PMID 20205229
39. Kennedy AS, Dezarn WA, McNeillie P, et al. Radioembolization for unresectable neuroendocrine hepatic metastases using resin 90Y-microspheres: early results in 148 patients. *Am J Clin Oncol.* Jun 2008;31(3):271279. PMID 18525307
40. Memon K, Lewandowski RJ, Mulcahy MF, et al. Radioembolization for neuroendocrine liver metastases: safety, imaging, and long-term outcomes. *Int J Radiat Oncol Biol Phys.* Jul 1 2012;83(3):887-894. PMID 22137020
41. Paprottka PM, Hoffmann RT, Haug A, et al. Radioembolization of symptomatic, unresectable neuroendocrine hepatic metastases using yttrium-90 microspheres. *Cardiovasc Intervent Radiol.* Apr 2012;35(2):334-342. PMID 21847708
42. Peker A, Cicek O, Soydal C, et al. Radioembolization with yttrium-90 resin microspheres for neuroendocrine tumor liver metastases. *Diagn Interv Radiol.* Jan-Feb 2015;21(1):54-59. PMID 25430526
43. Jia Z, Paz-Fumagalli R, Frey G, et al. Single-institution experience of radioembolization with yttrium-90 microspheres for unresectable metastatic neuroendocrine liver tumors. *J Gastroenterol Hepatol.* Sep 2017;32(9):1617-1623. PMID 28132407
44. Fan KY, Wild AT, Halappa VG, et al. Neuroendocrine tumor liver metastases treated with yttrium-90 radioembolization. *Contemp Clin Trials.* Sep 2016;50:143-149. PMID 27520932
45. Tice J. *Selective internal radiation therapy or radioembolization for inoperable liver metastases from colorectal cancer* San Francisco, CA: California Technology Assessment Forum; 2010.
46. Saxena A, Bester L, Shan L, et al. A systematic review on the safety and efficacy of yttrium-90 radioembolization for unresectable, chemorefractory colorectal cancer liver metastases. *J Cancer Res Clin Oncol.* Apr 2014;140(4):537-547. PMID 24318568
47. 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. *Ann Oncol.* Dec 2001;12(12):1711-1720. PMID 11843249
48. 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. *J Clin Oncol.* Aug 10 2010;28(23):3687-3694. PMID 20567019
49. Rosenbaum CE, Verkooijen HM, Lam MG, et al. Radioembolization for treatment of salvage patients with colorectal cancer liver metastases: a systematic review. *J Nucl Med.* Nov 2013;54(11):1890-1895. PMID 24071510
50. Van Hazel G, Blackwell A, Anderson J, et al. Randomised phase 2 trial of SIR-Spheres plus fluorouracil/leucovorin chemotherapy versus fluorouracil/leucovorin chemotherapy alone in advanced colorectal cancer. *J Surg Oncol.* Nov 1 2004;88(2):78-85. PMID 15499601
51. Townsend A, Price T, Karapetis C. Selective internal radiation therapy for liver metastases from colorectal cancer. *Cochrane Database Syst Rev.* Oct 07 2009(4):CD007045. PMID 19821394
52. 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):17231731. PMID 26903575

53. Salem R, Lewandowski RJ, Mulcahy MF, et al. Radioembolization for hepatocellular carcinoma using Yttrium-90 microspheres: a comprehensive report of long-term outcomes. *Gastroenterology.* Jan 2010;138(1):52-64. PMID 19766639
54. Seidensticker R, Denecke T, Kraus P, et al. Matched-pair comparison of radioembolization plus best supportive care versus best supportive care alone for chemotherapy refractory liver-dominant colorectal metastases. *Cardiovasc Intervent Radiol.* Oct 2012;35(5):1066-1073. PMID 21800231
55. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Colon Cancer. Version 2.2018. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed June 27, 2018.
56. Kennedy AS, Salem R. Radioembolization (yttrium-90 microspheres) for primary and metastatic hepatic malignancies. *Cancer J.* Mar-Apr 2010;16(2):163-175. PMID 20404614
57. Smits ML, Prince JF, Rosenbaum CE, et al. Intra-arterial radioembolization of breast cancer liver metastases: a structured review. *Eur J Pharmacol.* Jun 5 2013;709(1-3):37-42. PMID 23545356
58. Pieper CC, Meyer C, Wilhelm KE, et al. Yttrium-90 radioembolization of advanced, unresectable breast cancer liver metastases-a single-center experience. *J Vasc Interv Radiol.* Sep 2016;27(9):1305-1315. PMID 27461588
59. Gordon AC, Gradishar WJ, Kaklamani VG, et al. Yttrium-90 radioembolization stops progression of targeted breast cancer liver metastases after failed chemotherapy. *J Vasc Interv Radiol.* Oct 2014;25(10):1523-1532, 1532 e1521-1522. PMID 25156827
60. Saxena A, Kapoor J, Meteling B, et al. Yttrium-90 radioembolization for unresectable, chemoresistant breast cancer liver metastases: a large single-center experience of 40 patients. *Ann Surg Oncol.* Apr 2014;21(4):12961303. PMID 24337647
61. Cianni R, Pelle G, Notarianni E, et al. Radioembolisation with (90)Y-labelled resin microspheres in the treatment of liver metastasis from breast cancer. *Eur Radiol.* Jul 2013;23(1):182-189. PMID 22836160
62. Haug AR, Tiega Donfack BP, Trumm C, et al. 18F-FDG PET/CT predicts survival after radioembolization of hepatic metastases from breast cancer. *J Nucl Med.* Feb 2012;53(3):371-377. PMID 22331219
63. Jakobs TF, Hoffmann RT, Fischer T, et al. Radioembolization in patients with hepatic metastases from breast cancer. *J Vasc Interv Radiol.* May 2008;19(5):683-690. PMID 18440456
64. Bangash AK, Atassi B, Kaklamani V, et al. 90Y radioembolization of metastatic breast cancer to the liver: toxicity, imaging response, survival. *J Vasc Interv Radiol.* May 2007;18(5):621-628. PMID 17494843
65. Coldwell DM, Kennedy AS, Nutting CW. Use of yttrium-90 microspheres in the treatment of unresectable hepatic metastases from breast cancer. *Int J Radiat Oncol Biol Phys.* Nov 1 2007;69(3):800-804. PMID 17524567
66. Xing M, Prajapati HJ, Dhanasekaran R, et al. Selective internal Yttrium-90 radioembolization therapy (90Y-SIRT) versus best supportive care in patients with unresectable metastatic melanoma to the liver refractory to systemic therapy: safety and efficacy cohort studys. *Am J Clin Oncol.* Feb 2017;40(1):27-34. PMID 25089529
67. Eldredge-Hindy H, Ohri N, Anne PR, et al. Yttrium-90 microsphere brachytherapy for liver metastases from uveal melanoma: clinical outcomes and the predictive value of fluorodeoxyglucose positron emission tomograph. *Am J Clin Oncol.* Apr 2016;39(2):189-195. PMID 24441583
68. Gonsalves CF, Eschelman DJ, Sullivan KL, et al. Radioembolization as salvage therapy for hepatic metastasis of uveal melanoma: a single-institution experience. *AJR Am J Roentgenol.* Feb 2011;196(2):468-473. PMID 21257902
69. Kennedy AS, Nutting C, Jakobs T, et al. A first report of radioembolization for hepatic metastases from ocular melanoma. *Cancer Invest.* Jul 2009;27(6):682-690. PMID 19219675
70. Klingenstein A, Haug AR, Zech CJ, et al. Radioembolization as locoregional therapy of hepatic metastases in uveal melanoma patients. *Cardiovasc Intervent Radiol.* Feb 2013;36(1):158-165. PMID 22526099
71. Piduru SM, Schuster DM, Barron BJ, et al. Prognostic value of 18f-fluorodeoxyglucose positron emission tomography-computed tomography in predicting survival in patients with unresectable metastatic melanoma to the liver undergoing yttrium-90 radioembolization. *J Vasc Interv Radiol.* Jul 2012;23(7):943-948. PMID 22609292
72. Michl M, Haug AR, Jakobs TF, et al. Radioembolization with Yttrium-90 microspheres (SIRT) in pancreatic cancer patients with liver metastases: efficacy, safety and prognostic factors. *Oncology.* Jan 2014;86(1):24-32. PMID 24401529
73. Miller MD, Sze DY, Padia SA, et al. Response and overall survival for yttrium-90 radioembolization of hepatic sarcoma: a multicenter retrospective study. *J Vasc Interv Radiol.* Jun 2018;29(6):867-873. PMID 29724518
74. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. Version 2.2018.

https://www.nccn.org/professionals/physician_gls/PDF/neuroendocrine.pdf. Accessed June 27, 2018.