

Selective Internal Radiation Therapy

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Medical Guideline Disclaimer

The treating physician or primary care provider must submit to EmblemHealth the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care. EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public

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Definition

Selective Internal Radiation Therapy (SIRT) — also referred to as radioembolization or yttrium-90 (Y-90) hepatic brachytherapy, is an outpatient transcatheter interventional technique whereby radioactive particles (Y-90 microspheres) are delivered directly to the liver tumor bed via the hepatic artery. Once implanted, the microspheres emit localized radiation.

FDA-approved radioactive microspheres include SIR-Spheres[®] (biocompatible) and TheraSphere[®] (insoluble glass).

Guideline

- I. Selective internal radiation therapy (SIRT) is considered medically necessary when the following criteria are met:
 - A. Unresectable and/or medically inoperable primary or metastatic liver malignancies
 - 1. Unresectable liver only or liver dominant metastases from neuroendocrine tumors (e.g., carcinoids, pancreatic islet cell tumors, endocrine (tumor)
 - 2. Unresectable primary hepatocellular carcinoma (HCC)
 - 3. Unresectable metastatic liver tumors from primary colorectal cancer
 - 4. Treatment of unresectable liver metastases from breast carcinoma, ocular melanoma, cutaneous melanoma, or intrahepatic cholangiocarcinoma in the absence of available

systemic or liver-directed treatment options to relieve symptoms and/or possibly extend life expectancy

- B. The tumor burden should be liver dominant, not necessarily exclusive to the liver
- C. Eastern Cooperative Oncology Group (ECOG) performance status should be 0 or 1 or Karnofsky Performance Status (KPS) of 70 or more
- D. Life expectancy should be at least 3 months
- E. Radioactive Yttrium-90 (90Y) microspheres treatment is allowed only in the outpatient setting unless the documentation supports the medical necessity of inpatient treatment
- II. Repeat radioembolization is considered medically necessary for new or progressive primary or metastatic liver cancers when:
 - A. The member has had a previous satisfactory response to an initial radioembolization treatment as evidenced on results of a computed tomography (CT) scan or positron emission tomography (PET)-CT scan performed 3 months following the previous procedure. Response should be graded according to the revised RECIST guideline (Version 1.1)
 - B. The disease still must be liver dominant
 - C. Life expectancy of at least 3 months
 - D. ECOG performance status no greater than 2 or KPS of 70 or more
 - E. There are no other effective systemic or liver-directed treatment options
 - F. The member has compensated liver function tests (LFTs)
 - G. Estimated lung dose and combined lung dose from previous embolizations are within acceptable dose volume constraints. Exclude an individual with lung shunting in which the lung radiation dose is greater than 25 to 30 Gy per treatment or greater than 50 Gy cumulatively for all treatments
 - H. Treatment should be given to a targeted tumor volume
 - I. Repeat whole liver irradiation is considered experimental, investigational, or unproven (EIU) and will not be certified
 - J. Requests for a third radioembolization will not be certified
 - K. All requests for repeat radioembolization are subject to medical review

Limitations/Exclusions

Only FDA-approved microspheres will be considered medically necessary.

Requests for the treatment of liver metastases from other primary malignancies, including breast carcinoma, ocular melanoma, cutaneous melanoma, and intrahepatic cholangiocarcinoma, will be considered on a case-by-case basis. These requests should be based on the lack of any known systemic or liver-directed treatment options for the member in an effort to relieve symptoms and/or possibly extend life expectancy.

Radioactive Yttrium-90 (90Y) microspheres treatment is allowed only in the outpatient setting unless the documentation supports the medical necessity of inpatient treatment.

Revision History

May 7, 2021	Added covered indication for treatment of unresectable liver metastases from breast carcinoma, ocular melanoma, cutaneous melanoma, or intrahepatic cholangiocarcinoma
Mar. 8, 2019	Added repeat radioembolization criteria
Oct. 9, 2015	Added ECOG performance score prerequisite and life expectancy language
Aug. 20, 2009	Added hepatoma

Applicable Procedure Codes

37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction
75894	Transcatheter therapy, embolization, any method, radiological supervision and interpretation
77778	Interstitial radiation source application; complex
79445	Radiopharmaceutical therapy, by intra-arterial particulate administration
Q3001	Radioelements for brachytherapy, any type, each
S2095	Transcatheter occlusion or embolization for tumor destruction, percutaneous, any method, using yttrium-90 microspheres

Applicable ICD-10 Diagnosis Codes

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
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct

References

- Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. American Association for Study of Liver Disease (AASLD) Practice Guideline. Hepatology. 2011 Mar; 53(3):1020-1022. <u>http://onlinelibrary.wiley.com/doi/10.1002/hep.24199/epdf.</u> Accessed May 15, 2025.
- Cheng AL, Kang YK, Chen Z. et al. Efficacy and safety of sorafenib in patients in the Asia-Pacific region with advanced hepatocellular carcinoma: a phase III randomized, double-blind, placebo-controlled trial. Lancet Oncol. 2009 Jan; 10(1):25-34. <u>http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(08)70285-7/fulltext.</u> Accessed May 15, 2025.
- Chua TC, Bester L, Saxena A et al. Radioembolization and systemic chemotherapy improves response and survival for unresectable colorectal liver metastases. J Cancer Res Clin Oncol. 2011 May; 137(5):865-873. <u>http://link.springer.com/article/10.1007/s00432-010-0948-y.</u> Accessed May 15, 2025.

- Coldwell D, Sangro B, Salem R, et al. Radioembolization in the treatment of unresectable liver tumors: experience across a range of primary cancers. Am J Clin Oncol. 2012 Apr; 35(2):167-77. <u>http://journals.lww.com/amjclinicaloncology/Abstract/2012/04000/Radioembolization in the Treatment of Unre</u> sectable.15.aspx. Accessed May 15, 2025.
- Deleporte A, Flamen P, Hendlisz A. State of the art: radiolabeled microspheres treatment for liver malignancies. Expert Opin Pharmacother. 2010 Mar; 11(4):579-86. http://informahealthcare.com/doi/abs/10.1517/14656560903520916?journalCode=eop. Accessed May 15, 2025.
- Gray B, Van Hazel G, Hope M, et al. Randomized trial of SIR-Spheres[®] plus chemotherapy vs. chemotherapy alone for treating patients with liver metastases from primary large bowel cancer. Ann Oncol 2001; 12(12):1711-1720. <u>http://annonc.oxfordjournals.org/content/12/12/1711.full.pdf+html</u>. Accessed May 15, 2025.
- 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. 2010 Aug 10; 28(23):3687-3694. <u>http://jco.ascopubs.org/content/28/23/3687.</u> Accessed May 15, 2025.
- Hong K, Akinwande O, Bodei L, Chamarthy MR, Devlin PM, Elman S, Ganguli S, Kennedy AS, Koo SJ, Ouhib Z, Padia SA, Salem R, Selwyn RG, Yashar CM, Yoo DC, Zaki BI, Hartford AC, Trimmer CK. ACR-ABS-ACNM-ASTRO-SIR-SNMMI practice parameter for selective internal radiation therapy or radioembolization for treatment of liver malignancies. Brachytherapy. 2021 May-Jun;20(3):497-511. doi: 10.1016/j.brachy.2021.01.006. Epub 2021 Apr 3. PMID: 33824051.
- 9. Kennedy AS, Dezam WA, McNeillie P, et al. Radioembolization for unresectable neuroendocrine hepatic metastases using resin 90Y-microspheres: early results in 148 patients. Am J Clin Oncol. 2008 Jun; 31(3):271-279. <u>http://journals.lww.com/amjclinicaloncology/Abstract/2008/06000/Radioembolization_for_Unresectable_Neuroen_docrine.12.aspx.</u> Accessed May 15, 2025.
- 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. Int J Radiat Oncol Biol Phys. 2007 May 1; 68(1):13-23. <u>http://www.redjournal.org/article/S0360-3016(07)00097-1/abstract</u>. Accessed May 15, 2025.
- King J, Quinn R, Glenn DM, et al. Radioembolization with selective internal radiation microspheres for neuroendocrine liver metastases. Cancer. 2008 Sep 1; 113(5):921-929. http://onlinelibrary.wiley.com/doi/10.1002/cncr.23685/full. Accessed May 15, 2025.
- Kouri BE, Abrams RA, Al-Refaie WB, et al. ACR Appropriateness Criteria[®] radiologic management of hepatic malignancy. Date of origin 2007. Last review date 2015. <u>https://acsearch.acr.org/docs/69379/Narrative/.</u> Accessed May 15, 2025.
- Kulik LM, Atassi B, van Holsbeeck L, et al. Yttrium-90 microspheres (TheraSphere[®]) treatment of unresectable hepatocellular carcinoma: downstaging to resection, RFA and bridge to transplantation. J Surg Oncol. 2006 Dec 1; 94(7):572-586. <u>http://onlinelibrary.wiley.com/doi/10.1002/jso.20609/abstract.</u> Accessed May 15, 2025.
- Kulick LM, Carr BI, Mulcahy MF, et al. Safety and efficacy of ⁹⁰Y radiotherapy for hepatocellular carcinoma with and without portal vein thrombosis. Hepatology. 2008 Jan; 47(1):71-81. <u>http://onlinelibrary.wiley.com/doi/10.1002/hep.21980/full</u>. Accessed May 15, 2025.
- Lam MGEH, Abdelmaksoud MH, Chang DT, et al. Safety of ⁹⁰Y radioembolization in patients who have undergone previous external beam radiation therapy. Int J Radiat Oncol Biol Phys. 2013 Oct 1; 87(2):323-329. <u>http://www.redjournal.org/article/S0360-3016(13)00634-2/abstract.</u> Accessed May 15, 2025.
- Lau WY, Kennedy AS, Kim YH, et al. Patient selection and activity planning guide for selective internal radiotherapy with Yttrium-90 resin microspheres. Int. J Radiat Oncol Biol Phys 2012 Jan 1; 82(1):401-407. <u>http://www.sciencedirect.com/science/article/pii/S0360301610030610.</u> Accessed May 15, 2025.
- 17. Lau WY, Lai ECH, Leung TWT. Current role of selective internal irradiation with Yttrium-90 microspheres in the management of hepatocellular carcinoma: a systematic review. In June 15, 2023.
- 18. t. J. Radiat Oncol Biol Phys. 2011 Oct 1; 81(2):460-467. <u>http://www.redjournal.org/article/S0360-3016(10)00819-9/abstract.</u> Accessed May 15, 2025.

- Lewandowski RJ, Kulik, LM, Riaz A, et al. A comparative analysis of transarterial downstaging for hepatocellular carcinoma: chemoembolization versus radioembolization. Am J Transplant. 2009 Aug 9; 9(8):1920–1928. http://onlinelibrary.wiley.com/doi/10.1111/j.1600-6143.2009.02695.x/full. Accessed May 15, 2025.
- Llovet JM , Di Bisceglie AM, Bruix J. et al., Design and endpoints of clinical trials in hepatocellular carcinoma. J Natl Cancer Inst 2008 May 21; 100(10):698-711. <u>http://jnci.oxfordjournals.org/content/100/10/698.full.pdf+html.</u> Accessed May 15, 2025.
- 21. Llovet JM, Ricci S, Mazzaferro V, et al., Sorafenib in advanced hepatocellular carcinoma N Engl J Med. 2008 Jul 24; 359(4):378-390. <u>http://www.nejm.org/doi/full/10.1056/NEJMoa0708857.</u> Accessed May 15, 2025.
- Mazzaferro V, Regalia, E, Doci R, et al., Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med. 1996 Mar 14; 334(11):693-700. <u>http://www.nejm.org/doi/full/10.1056/NEJM199603143341104#t=abstract.</u> Accessed May 15, 2025.
- 23. National Comprehensive Cancer Network (NCCN) Guidelines. Biliary Tract Cancers. V2.2024. https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf. Accessed May 15, 2025.
- 24. National Comprehensive Cancer Network (NCCN) Guidelines. Hepatobiliary Carcinoma. V1 2024. https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf. Accessed May 15, 2025.
- Nichols EM, Grabowski S, Hanlon A et al. Performance status (PS), number of lesions and interval from metastatic diagnosis treatment (IMDTT) predict for overall survival (OS) in patients treated with hepatic transarterial radioembolization (TARE) with Yttrium-90 (Y⁹⁰) microspheres. Int J Radiat Oncol Biol Phys. 2011 Oct 1; 81(2 Suppl):S346–S347. Abstract 2281. <u>http://www.redjournal.org/article/S0360-3016(11)02650-2/pdf.</u> Accessed May 15, 2025.
- 26. 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 Jan; 138(1):52-64. http://www.sciencedirect.com/science/article/pii/S0016508509015741. Accessed May 15, 2025.
- Salem R., Thurston KG. Radioembolization with ⁹⁰Yttrium microspheres: a state-of-the-art brachytherapy treatment for primary and secondary liver malignancies. Part 1: technical and methodological considerations. J Vasc Interv Radiol. 2006 Aug; 17(8):1251-1278. <u>http://www.jvir.org/article/S1051-0443(07)60901-4/abstract.</u> Accessed May 15, 2025.
- Salem R., Thurston KG. Radioembolization with ⁹⁰Yttrium microspheres: a state-of-the-art brachytherapy treatment for primary and secondary liver malignancies. Part 2: special topics. J Vasc Interv Radiol. 2006 Sep; 17(9):1425-1439. <u>http://www.jvir.org/article/S1051-0443(07)60924-5/abstract.</u> Accessed May 15, 2025.
- Sangro B, Bilbao JI, Boan J, et al., Radioembolization using 90Y-resin microspheres for patients with advanced hepatocellular carcinoma. Int J Radiat Oncol Biol Phys. 2006 Nov 1; 66(3):792-800. <u>http://www.redjournal.org/article/S0360-3016(06)00958-8/abstract.</u> Accessed May 15, 2025.
- 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. 2014 Apr; 140(4):537-547. <u>http://link.springer.com/article/10.1007/s00432-013-1564-4.</u> Accessed May 15, 2025.
- Schwarz RE, Abou-Alfa GK, Ghassan K., et al., Nonoperative therapies for combined modality treatment of hepatocellular cancer: expert consensus statement. HPB (Oxford) 2010 Jun, 12(5):313–320. <u>http://onlinelibrary.wiley.com/doi/10.1111/j.1477-2574.2010.00183.x/abstract.</u> Accessed May 15, 2025.
- SIR-Spheres[®] Microspheres Bibliography: September 2013. <u>http://foxfireglobal.sirtex.com/sites/foxfireglobal.sirtex.com/files/user/sir-spheres_publications_774-u-1013.pdf.</u> Accessed May 15, 2025.
- SIR-Spheres[®] microspheres (Yttrium-90 Microspheres). Package insert. Sirtex Medical Inc. Wilmington MA. U.S. Food and Drug Administration (FDA). Updated January 23, 2003. Accessed March 19, 2019. <u>http://www.accessdata.fda.gov/cdrh_docs/pdf/P990065c.pdf</u>. Accessed May 15, 2025.
- TheraSphere[®] Yttrium-90 Glass Microspheres). Package insert. BTG International Group. U.S. Food and Drug Administration (FDA). Humanitarian Device Exemptions. Updated January 4, 2000. <u>http://www.accessdata.fda.gov/cdrh_docs/pdf/H980006c.pdf.</u> Accessed May 15, 2025.

- 35. Tsai AL, Burke CT, Kennedy AS, et al. Use of yttrium-90 microspheres in patients with advanced hepatocellular carcinoma and portal vein thrombosis. J Vasc Interv Radiol. 2010 Sep; 21(9):1377-1384. <u>http://www.jvir.org/article/S1051-0443(10)00508-7/abstract.</u> Accessed May 15, 2025.
- 36. Specialty-matched clinical peer review.