Transarterial Radioembolization (TARE)/ Selective Internal Radiation Therapy (SIRT) for the Treatment of Malignant Cancers of the Liver

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➲ Instructions for Use

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Community Plan Policy

- Transarterial Radioembolization (TARE)/Selective Internal Radiation Therapy (SIRT) for the Treatment of Malignant Cancers of the Liver

Application

UnitedHealthcare Commercial

This Medical Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Policy applies to Individual Exchange benefit plans.

Coverage Rationale

Note: This policy applies to individuals 19 years of age or older. Transarterial Radioembolization (TARE)/selective internal radiation therapy (SIRT) is covered without further review for individuals younger than 19 years of age.

Transarterial Radioembolization (TARE)/selective internal radiation therapy (SIRT) using yttrium-90 microspheres is proven and medically necessary for the following indications in individuals with an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2:

- Liver-dominant primary hepatocellular carcinoma in individuals who are not surgical candidates
- Primary hepatocellular carcinoma as a bridge to liver transplant
- Liver metastases from neuroendocrine tumors in individuals who are not surgical candidates when systemic therapy has failed to control symptoms
- Liver metastases from colorectal carcinoma in individuals with chemotherapy-resistant or Refractory disease and with predominant hepatic metastases
- Liver metastases from intrahepatic cholangiocarcinoma in individuals who are not surgical candidates
- Metastasis from uveal melanoma when confined to the liver

Transarterial Radioembolization (TARE)/selective internal radiation therapy (SIRT) using yttrium-90 microspheres is unproven and not medically necessary for all other indications due to insufficient evidence of efficacy.

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Medical Records Documentation Used for Reviews

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the service requested; refer to the guidelines titled Medical Records Documentation Used for Reviews.

Definitions

Eastern Cooperative Oncology Group (ECOG) Scale of Performance Status: A standard criterion for measuring how the disease impacts a person's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (e.g., walking, working, etc.).

Grade	ECOG Performance Status
0	Fully active, able to carry on all predisease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair
5	Dead

Limited Extrahepatic Disease: Metastases limited to the lung with less than five nodules with ≤ 1-cm diameter or a single nodule ≤ 1.7-cm diameter and/or a single area of lymph node involvement < 2-cm diameter (Wasan et al., 2017).

Refractory: Cancer that does not respond to treatment. The cancer may be resistant at the beginning of treatment, or it may become resistant during treatment. Also called resistant cancer (National Cancer Institute, 2021).

Transarterial Radioembolization (TARE): An intra-arterial cancer therapy that uses radioactive microspheres impregnated with yttrium-90 which are directly injected into the hepatic artery. Also called radioembolization and selective internal radiation therapy (Choi and Kim, 2022).

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other policies and guidelines may apply.

CPT Code	Description
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
79445	Radiopharmaceutical therapy, by intra-arterial particulate administration

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

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Description of Services

Transarterial Radioembolization (TARE), also known as selective internal radiation therapy (SIRT), using Yttrium-90 is a minimally invasive, catheter-directed therapy that delivers localized radiation to hepatic tumors through selective arterial injection in the angiography suite. By concentrating radiation within tumor tissue, this treatment aims to achieve effective local control while minimizing injury to normal liver. TARE is an important component of multidisciplinary management for primary liver cancer and carefully selected cases of liver-dominant metastatic disease, particularly in patients who are not candidates for curative surgical or ablative therapies or who have progressed on or are intolerant to systemic therapies such as chemotherapy.

Clinical Evidence

Clinical Practice Guideline

American Association of Physicists in Medicine (AAPM)

The 2023 AAPM practice guideline states that the following should be taken into consideration when selecting appropriate candidates for yttrium-90 (Y-90) radioembolization to minimize the risk of severe or fatal toxicity:

- Contrast-enhanced liver protocol computed tomography (CT) or magnetic resonance imaging (MRI) should be used to determine lesion burden and identification of imaging factors associated with poor prognosis such as ascites.
- Patients' bilirubin should be < 2 mg/dL and ideally below 1.3 mg/dL if lobar or bilobar treatment is planned. Variations with higher levels of bilirubin may be acceptable when selective radiation segmentectomy is performed.
- Decreasing albumin levels forecast impending liver dysfunction, and albumin levels of > 3 g/dL are associated with improved survival post TARE.
- Relative contraindications include:
  - Significantly decompensated liver function (e.g., Child-Pugh score ≥ B8)
  - Greater than 70% to 75% liver involvement by tumor
  - Poor performance status
  - Pregnancy
  - High lung shunt fraction
- The following are indicators of poor outcomes:
  - Presence of ascites, especially uncontrolled
  - Infiltrative disease with a tumor burden of > 50%
  - Eastern Cooperative Oncology Group (ECOG) performance status of > 2
  - Patients with cirrhosis with a liver volume of < 1.5 L
- Prior radiation therapy to the liver requires careful planning to ensure patient safety. Radioembolization may be reasonable, especially if given in a segmental fashion after careful assessment of the prior absorbed dose delivered to the liver. Prior therapies can affect residual liver function and predispose the patient to radioembolization-induced liver disease.

Liver Metastases From Colorectal Cancer

Schneider et al. (2025) conducted a single-center retrospective study that evaluated high-dose transarterial radioembolization (TARE) using Y-90 resin microspheres for hepatic metastases between May 2019 and April 2025. Overall, 15 patients were included in the study. The median age was 66 years, 53.3% were male, and the primary tumors originated from colorectal, neuroendocrine, and breast cancers. Treatment planning targeted a mean tumor dose of at least 150 Gy, with a median administered activity of 2.2 GBq and a median posttreatment tumor absorbed dose of 160.7 Gy. The primary outcomes were treatment efficacy and toxicity, with efficacy assessed by radiological response using Response Evaluation Criteria in Solid Tumors (RECIST 1.1), time to progression (TTP), overall survival (OS), and toxicity graded by Common Terminology Criteria for Adverse Events (CTCAE v5.0); analyses used Kaplan-Meier estimation and R software. The results showed that disease control was achieved in all patients at 3 months, with partial response in 66.7%, stable disease in 33.3%, median OS of 26.5 months (95% CI, 24.5 months to no estimate), and grade 3 toxicity in 13.3% of patients. The authors concluded that high-dose TARE using Y-90 resin microspheres was safe and effective for hepatic metastases from various primary malignancies and achieved high disease control rates (DCRs) and favorable tolerance, even in pretreated patients. This study is limited by the retrospective design, small sample size, and heterogeneity in the study population, tumor origins, and treatment histories.

An ECRI Clinical Evidence Assessment (2021a) report on TARE for treating metastases to the liver focused on TARE's safety and effectiveness in treating unresectable metastatic liver tumors and how they compare with those of other treatment modalities. The report included three systematic reviews and three meta-analyses that pooled evidence from

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randomized controlled trials (RCTs), melanoma (one systematic review), breast cancer (one systematic review), and neuroendocrine tumors (two systematic reviews). In individuals with chemotherapy-refractory colorectal cancer metastasis who received TARE as third-line therapy, TARE with Y-90 improved OS compared with best supportive care. In individuals with colorectal cancer metastasis, adding TARE to first-line treatment did not improve survival. OS was higher with transarterial chemoembolization (TACE) than with TARE in individuals with neuroendocrine tumor metastasis based on evidence from one systematic review. The systematic review included only six retrospective cohort studies at a high risk of selection bias. In individuals with melanoma and breast cancer metastasis, there was a lack of comparative outcomes for OS, which prevented analysis of TARE's safety and effectiveness. One guideline recommended TARE with chemotherapy in all second-line or later treatment settings for colorectal cancer metastasis, and two guidelines stated that TARE should be considered as a treatment option as a second-line or later treatment for colorectal cancer metastasis

Mulcahy et al. (2021) conducted a randomized, open-label, international, multicenter, phase 3 trial regarding radioembolization with chemotherapy for colorectal liver metastases. The study evaluated the impact of transarterial Y-90 radioembolization in combination with second-line systemic chemotherapy for colorectal liver metastases. Between May 2012 and August 2020, 428 participants from 95 centers in North America, Asia, and Europe were randomly assigned either to chemotherapy with or without TARE. Of the 215 participants who were assigned to the TARE group, 187 received TARE, 16 received only chemotherapy, and 12 received no treatment. The control group consisted of 213 participants; 191 received second-line chemotherapy, and 22 received no therapy. The median time to TARE was 25 days from the time of assignment, with median overall follow-up at 36 and 42.3 months. The median OS was 14.0 and 14.4 months in the TARE and chemotherapy groups, respectively. The objective response rate (ORR) was 34% and 21.1% in the TARE and chemotherapy groups, respectively. DCRs were 79.5% and 72.8% in the TARE and chemotherapy groups, respectively. There was a benefit in PFS seen with TARE in those with no detectable extrahepatic lesions and those with extrahepatic benign lesions. The study concluded that adding TARE for systemic therapy for second-line colorectal liver metastases leads to longer PFS.

Baltatzis and Siriwardena (2019; included in the 2021a ECRI report) conducted a systematic review that included four randomized trials and eight clinical cohort series. The study population comprised 120 individuals who were undergoing liver resection after chemotherapy and selective internal radiation therapy (SIRT). The conversion rate to hepatectomy in individuals with previously unresectable disease was 13.6%. The interval from SIRT to surgery ranged from 39 days to 9 months. The longest survivor was reported at 96 months after hepatectomy. There were four deaths (3.3%) after hepatectomy among individuals who were treated with chemotherapy and SIRT. The authors concluded that the study showed that 13.6% of individuals with initially inoperable disease underwent resection with low procedure-related mortality. (Authors Cosimelli et al., 2010, Hendlisz et al., 2010, and Maleux et al., 2016, previously discussed in this policy, are included in this review.)

Kalva et al. (2017) conducted a retrospective study to report the safety and survival outcomes of Y-90 radioembolization when used as salvage therapy for chemotherapy-resistant liver mCRC. Overall, 45 patients with hepatic mCRC underwent Y-90 radioembolization after failure of systemic chemotherapy. Y-90 radioembolization was technically successful in all. Overall, 23 patients had no toxicities, six had grade 3 toxicities, and there were no grade 4 toxicities. Two patients died within 30 days of treatment from renal failure that was unrelated to the procedure. One patient had partial response, 34 had stable disease, and six had progressive disease. Positron emission tomography (PET) response was seen in 46% of them, with two patients (4%) having complete and 22 (42%) having partial metabolic response. The median survival was 186 days. Those who had response on PET following Y-90 treatment had a median OS of 317 days, whereas patients with no response on PET had a median OS of 163 days. The authors concluded that Y-90 radioembolization as a salvage therapy for chemotherapy-resistant hepatic mCRC is safe and resulted in disease stability.

Wasan et al. (2017; included in the 2021a ECRI report) performed a combined analysis of the FOXFIRE, SIRFLOX, and FOXFIRE-Global randomized studies to evaluate the efficacy of combining first-line chemotherapy with SIRT using Y-90 resin microspheres in participants with mCRC with liver metastases. The studies were designed for combined analysis of OS. Chemotherapy-naive participants with mCRC with liver metastases that were not suitable for curative resection or ablation were randomly assigned (1:1) to either oxaliplatin-based chemotherapy FOLFOX (folinic acid, fluorouracil, and oxaliplatin; n = 549) or FOLFOX plus single-treatment SIRT concurrent with cycle 1 or 2 of chemotherapy (n = 554). The median follow-up was 43.3 months. There were 411 deaths in the FOLFOX-alone group and 433 deaths in the FOLFOX plus SIRT group. The median survival time in the FOLFOX plus SIRT group was 22.6 months compared with 23.3 months in the FOLFOX-alone group. Serious adverse events (AEs) of any grade occurred in 244 participants who were receiving FOLFOX alone and 274 receiving FOLFOX plus SIRT. The authors concluded that the OS was not significantly different between groups [hazard ratio (HR), 1.04; 95% CI 0.90-1.19]. They recommended further studies to study the role of SIRT in carefully selected populations and as a consolidation therapy after chemotherapy.

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Clinical Practice Guidelines

American Society of Clinical Oncology (ASCO)

In 2024, a multidisciplinary committee that comprised experts in medical oncology, hepatobiliary surgery, radiology, and nuclear medicine reviewed the published literature and made the following recommendations for treating patients with liver metastasis from colon cancer (González-Flores et al., 2024):

- In routine clinical practice, the use of Y-90 TARE in liver mCRC is intended for patients with predominantly hepatic disease that is refractory or intolerant to chemotherapy:
  - The clinical selection criteria for Y-90 TARE should include laboratory examinations, including blood count, coagulation, liver, and renal profile
  - Prognostic markers such as carcinoembryonic antigen should also be evaluated
  - Evaluation of the patient's treatment history, including previous surgeries and local treatments such as chemoembolization (TACE) and/or local ablation techniques
- Absolute contraindications for treatment:
  - Pregnancy and lactation
  - Life expectancy of < 3 months
  - Clinical hepatic impairment
  - Disseminated extrahepatic disease
- Relative contraindications to treatment:
  - Elevated Child-Pugh score (> 7 with an increased likelihood of hepatic decompensation)
  - Elevated intrahepatic (> 50%-70% replacement of liver parenchyma by the tumor) or extrahepatic tumor burden
  - Acute or severe chronic renal failure (creatinine clearance < 30 mL/min)
  - Previous external beam radiation therapy

In the 2023 guidelines for treating mCRC, the society gives the following recommendation: SIRT is not routinely recommended for patients with mCRC and unilobar or bilobar metastases of the liver (type: evidence-based, harms outweigh benefits; evidence quality: low; strength of recommendation: weak) (Morris et al., 2023).

American College of Radiology (ACR)

In the 2022 appropriateness criteria for the management of liver cancer, the ACR states that TARE may be appropriate for solitary colorectal liver metastasis and multifocal bilobar colorectal carcinoma, either liver dominant or isolated.

National Comprehensive Cancer Network® (NCCN®)

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for both colon and rectal cancers state the following:

- Y-90 microsphere selective internal radiation is an option in highly selected patients with chemotherapy-resistant/-refractory disease and with predominant hepatic metastases.
- Y-90 radioembolization (radiation lobectomy approach) can be considered instead of portal vein embolization when hepatic metastatic disease is not optimally resectable based on insufficient remnant liver volume or when there is borderline resectable disease that would benefit from tumor downsizing and remnant hypertrophy.

The use of arterial-directed therapies in highly selected patients is a category 2A recommendation category of evidence and consensus based on lower-level evidence. There is uniform NCCN consensus that the intervention is appropriate.

National Institute for Health and Care Excellence (NICE)

NICE states that SIRT is a potentially beneficial treatment for patients with nonresectable colorectal metastases in the liver. In people who cannot tolerate chemotherapy or have liver metastases that are refractory to chemotherapy, there is evidence of efficacy, but this is limited, particularly for important outcomes such as quality of life. In people who can have chemotherapy, evidence on OS and quality of life is inadequate in quality. This procedure should only be done by clinicians with specific training in SIRT. Further research should report details of patient selection, whether the primary colorectal tumor arose in the left or right side of the colon, extrahepatic disease, and tumor-to-liver volume. Outcomes should include survival and quality of life (NICE, 2020; updated 2024).

Liver Metastases From Neuroendocrine Tumors

Garrou et al. (2025) conducted a systematic review that followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol checklist to evaluate the prognostic role of TARE in individuals with neuroendocrine liver metastases over the past 25 years. Overall, 46 studies that included at least 20 individuals treated with TARE or in combination with other possible treatment options such as systemic treatment or different localized therapies were

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included. The studies each enrolled between 23 and 1,027 adults who were aged 25 to 91 years, with an overall total of 2,579. Statistical analyses were performed using Statistica 11, and the primary outcomes assessed were OS, hepatic PFS (HPFS), and imaging response assessed by RECIST 1.1 criteria. The results showed that there was a median OS of 33 months in 809 individuals and a median HPFS of 24 months in 414 individuals. Imaging response at 3 to 6 months demonstrated 28.6% complete or partial response, 57.8% stable disease, and 13.6% progression. The authors concluded that TARE may be an acceptable therapy for individuals with neuroendocrine liver metastases regardless of tumor type and histological characteristics. Gastroenteric and well-differentiated tumors, with limited tumor burden and no extrahepatic disease, show a better prognosis. This systematic review is limited due to overlapping data from the same registries or subsets of individuals. Additional research is needed to determine optimal selection of individuals and timing of the intervention.

Schaarschmidt et al. (2022; included in Garrou et al., 2025), in an international, multicenter, retrospective study, analyzed the use of Y-90 in patients with neuroendocrine neoplasms and hepatic metastases and the potential role of Y-90 in a multimodal treatment concept. Prior to Y-90 treatment, 297 angiographic evaluations in patients with neuroendocrine neoplasms took place and were analyzed. The outcomes measured were tumor response using RECIST 1.1 and survival data, with the OS between different groups compared using the Kaplan-Meier curves and log-rank test. The study results showed that after Y-90 radioembolization, the DCR, according to RECIST 1.1, was 83.5% after 3 months and 50.9% after 12 months. The OS in the entire population was 38.9 ±33.0 months. High tumor grade ($p < 0.006$) and high tumor burden ($p = 0.001$) were associated with a significant decrease in OS. The presence of extrahepatic metastases ($p = 0.335$) and the type of metastatic vascularization pattern ($p = 0.460$) had no influence on OS. Those who received Y-90 radioembolization as second-line therapy had slightly longer but not statistically significant OS than patients who had Y-90 radioembolization in a salvage setting (44.8 vs 30.6 months; $p = 0.078$). Hepatic and global PFS after Y-90 radioembolization significantly decreased in pretreated patients compared with patients with second-line therapy ($p = 0.011$ and $p = 0.010$, respectively). The authors concluded that Y-90 radioembolization could be an essential alternative to peptide receptor radionuclide therapy and second-line treatment in individuals with progressive, liver-dominant disease that was pretreated with somatostatin analogs. Limitations of the study include its retrospective nature and differences in procedural technique. A prospective study would support the authors' conclusions.

Egger et al. (2020; included in Garrou et al., 2025) conducted a retrospective multi-institutional review of literature that compared patients with unresectable neuroendocrine liver metastases who were undergoing TACE (n = 197) vs TARE with Y-90 (n = 51). The patients were scanned by CT every 6 months, along with tumor marker and clinical examinations. The median follow-up in the entire cohort was 34 months. There were no differences in overall morbidity (TARE, 13.7% vs TACE, 22.6%), grade III/IV complication (5.9% vs 9.2%), or 90-day mortality. There was no difference in median OS (35.9 vs 50.1 months) or PFS (15.9 vs 19.9 months). The authors concluded that both TACE and TARE with Y-90 are safe and effective methods for unresectable neuroendocrine liver metastases. TARE is associated with a shorter hospital stay, less liver toxicity, and fewer complications.

Cramer et al. (2016; included in Garrou et al., 2025) conducted a prospective longitudinal study to determine the effect of Y-90 radioembolization therapy on health-related quality of life (HRQOL) in participants with neuroendocrine tumor liver metastases (NETLMs). Baseline Short Form 36 HRQOL scores were evaluated for significant change at 1, 3, 6, 12, and 24 months following Y-90 radioembolization. OS times were calculated from first Y-90 radioembolization using the Kaplan-Meier method and analyzed using the log-rank test. Overall, 30 participants were enrolled in the study. At the 6- and 12-month follow-up, mean mental health and social functioning domain scores were significantly higher than baseline. The remainder of domains showed no significant difference at 6 or 12 months. Those with a baseline Mental Component Summary of over 50.0 had significantly longer mean survival than those with a score of under 50.0 (37.50 vs 18.19 months). Participants with a baseline Physical Component Summary over 50.0 had no significant difference in survival compared with those under 50.0 (38.09 vs 30.69 months). The authors concluded that participants with NETLMs treated with Y-90 had sustained HRQOL for up to 24 months following treatment. Temporary increases in mental health and social functioning at the medium-term follow-up were observed.

Barbier et al. (2016) conducted a retrospective study to evaluate the safety and efficacy of SIRT in patients with unresectable liver metastases from NETLMs. In 40 patients, 54 evaluable SIRT procedures were performed: 33 to the right liver lobe, 13 to the left lobe, and eight to both lobes. Late follow-up imaging (mean, 20 months) was performed after 44 treatments. Tumor response was evaluated according to the modified RECIST on CT or magnetic resonance images, and medical records were reviewed. Objective tumor response and DCRs were 54% and 94%, respectively, at the early follow-up examination (mean, 3 months) and 34% and 57% at the late follow-up examination. Mean OS from the first SIRT was 34.8 months, and survival rates at 1, 2, 3, and 5 years were 76%, 59%, 52%, and 35%, respectively. Adverse effects were generally mild and easily manageable, except in one patient who died from radiation-induced liver failure.

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The authors concluded that SIRT with Y-90 resin microspheres is a safe and effective treatment for progressive NETLMs. The study is limited by its retrospective observations and small sample size.

Clinical Practice Guidelines

NCCN

The NCCN Guidelines® on neuroendocrine and adrenal tumors principles of liver-directed therapy for tumor metastases state the following:

- TARE may be considered, particularly in the following scenarios:
  - Lobar or segmental (less than lobular) disease distribution
  - Patients with prior Whipple surgery or biliary tract instrumentation [lower risk of hepatobiliary infection than transarterial embolization (TAE)/TACE]
- TARE is better tolerated than TAE/TACE, but late radioembolization-induced chronic hepatotoxicity may occur in long-term survivors and is particularly a concern among patients who are undergoing bilobar radioembolization

National Institute for Health and Care Excellence (NICE)

In a 2024 interventional procedures guidance, NICE recommends SIRT as a treatment option for neuroendocrine tumors that have metastasized to the liver. Patient selection should be done by a multidisciplinary team with experience in managing neuroendocrine tumors and treatment conducted in specialized centers by trained and experienced clinicians (NICE, 2024).

Primary Hepatocellular Carcinoma

Lin and Tan (2026) conducted a systematic review and meta-analysis that evaluated the efficacy and safety of Y-90 TARE compared with those of conventional or systemic therapies (control) in individuals with advanced or unresectable hepatocellular carcinoma (HCC). Overall, 40 studies that involved over 10,000 individuals across multiple continents were included, most of which were retrospective (n = 33), with seven prospective design studies. The studies were analyzed using random-effects models to pool HRs and risk ratios. The studies included individuals with advanced disease, included comparator arms, and reported OS, PFS, or AEs, with sufficient data for hazard or odds ratio calculation. The primary outcomes were OS and PFS, as defined by pooled HRs. Safety was assessed by individuals who experienced a grade 3 or higher AE. The results showed that TARE significantly improved OS (HR, 3.14; 95% CI, 1.79-5.49; $p < 0.001$) and PFS (HR, 2.69; 95% CI, 1.65-4.39; $p < 0.001$) compared with control therapies. The pooled risk ratio for severe AEs was 0.75 (95% CI, 0.46-1.24; $p = 0.26$), indicating no significant increase in toxicity. Substantial heterogeneity is evident in the studies and reflects variations in study design, population characteristics, tumor burden, and dosimetric characteristics. However, subgroup analysis, particularly when stratified by liver function, showed therapeutic benefit of TARE, even in individuals with moderate liver impairment, which indicates the relative tolerability. The authors concluded that Y-90 TARE provides significant survival benefits and favorable safety outcomes in advanced HCC and is considered an effective locoregional therapy (LRT) that is suitable for integration into multidisciplinary management, particularly in individuals with preserved hepatic function or those who are unsuitable for systemic therapy. Furthermore, treatment goals differ, with higher doses needed for curative intent in early-stage disease. For advanced disease and impaired liver function, the focus is on liver preservation.

Chow et al. (2022) investigated the comparison between radiofrequency ablation (RFA), radiation therapy, TACE, and Y-90 for treating HCC through a systematic review and network meta-analysis of survival data. Using a multivariate network meta-analysis, the authors extracted survival data from Kaplan-Meier survival curves and meta-analyzed. The exploration acquired a total of 5,549 individuals in 24 RCTs or propensity score–matched observational studies. The results demonstrated that while 1-year OS was higher for Y-90 than TACE (RR, 0.85; 95% CI, 0.72-0.99), all other 1-year OS comparisons across the four modalities produced comparable OS, with no differences among the treatment modalities in 2-year and 3-year OS. TACE had a fair PFS advantage relative to RFA (RR, 0.81; 95% CI, 0.68-0.95) and radiation therapy (RR, 0.65; 95% CI, 0.51-0.83) at 2 years. The authors concluded that all modalities resulted in similar OS. (Salem et al., 2016, previously in this policy, is included in this review.)

Dhondt et al. (2022) conducted a single-center, prospective RCT (TRACE), in which Y-90 TARE was compared with doxorubicin-eluting bead TACE (DEB-TACE) in participants with intermediate-stage HCC and an ECOG performance status of 1 and participants with early-stage HCC who were not eligible for surgery or ablation. The outcomes measured were the TTP in the intention to treat (ITT) and per protocol. The participants were randomized to either the TARE arm (n = 38) or the DEB-TACE arm (n = 34). The results of the trial showed that the median TTP overall was 17.1 months in the TARE arm and 9.5 months in the DEB-TACE arm [ITT: HR, 0.36, 95% CI, 0.18-0.70, $p = 0.002$; per protocol (32 and 34 participants, respectively): HR, 0.29, 0.14-0.60; $p < 0.001$]. Median OS was 30.2 months after TARE and 15.6 months after DEB-TACE (ITT: HR, 0.48; 0.28-0.82; $p = 0.006$). Severe AEs of grade ≥ 3 occurred in 13 of 33 (39%) as opposed to

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19 of 36 (53%) after TARE and DEB-TACE, in that order (p = 0.47), and 30-day mortality was seen in zero of 33 (0%) opposed to three of 36 (8%) (p = 0.24); these were comparable for safety. In the interim, the HR for the primary end point of TTP of < 0.39 indicated the study's halt. The authors concluded that Y-90 radioembolization provides better tumor control and survival than the drug-eluting chemoembolization beads in specific individuals with early and intermediate HCC.

An ECRI (2021b) report evaluated TARE compared with other treatment modalities through systematic reviews and reported outcomes in individuals with unresectable primary liver tumors at different disease stages. The studies that were assessed consisted of two systematic reviews on TARE vs TACE, one systematic review regarding radiation therapy vs TARE, and two systematic reviews and one RCT on sorafenib vs TARE; studies on TARE alone included one systematic review and one systematic review in people with HCC, portal vein tumor thrombosis (PVT), and intrahepatic cholangiocarcinoma (ICC) and treatment with TARE. Findings included no difference in AEs between TARE and TACE as well as TARE and DEB-TACE. In comparing TARE and sorafenib for intermediate locally advanced HCC, the authors reported that the OS rate did not differ between treatment options. In individuals with intermediate locally advanced and advanced HCC, serious AEs occurred more often in the sorafenib group vs the TARE group. In those with advanced HCC, the authors reported that serious AEs occurred more often with SIRT and sorafenib than with sorafenib alone. When comparing TARE vs three-dimensional conformal radiotherapy vs stereotactic body radiotherapy, the stated 1-year survival rate did not vary statistically between people with HCC and PVT treated with TARE, three-dimensional conformal radiotherapy, or stereotactic body radiotherapy. Lastly, in comparing TARE in individuals with HCC and PVT, a median OS of 9.7 months after TARE in all people with HCC with PVT was reported. Limitations include differences in population, lack of generalization across studies or people, high risk for bias due to heterogeneity in the population, small size, and retrospective design. The authors concluded that TARE in individuals with HCC will improve OS rates compared with conventional TACE

ECRI evaluated TheraSphere® (Boston Scientific Corp.) for treating HCC through a Clinical Evidence Assessment. The assessment focused on the safety and effectiveness of TheraSphere compared with those of other treatments, such as TACE. The report summarized the evidence as somewhat favorable, concluding that TARE with TheraSphere is safe and increases time to disease progression compared with standard care in individuals with unresectable HCC. However, However, they further highlighted that the therapy improves liver transplant prospects but does not improve OS. Larger, multicenter RCTs that compare TheraSphere with other treatments would help confirm the therapy's safety and effectiveness (ECRI, 2021c).

Lemieux et al. (2021; included in the 2021c ECRI report) conducted a systematic review and meta-analysis of RCTs that compared Y-90 TARE with the standard of care for the nonsurgical treatment of HCC. The outcomes that were measured were OS, PFS, TTP, DCR, grade ≤ 3 AEs, and rates of gastrointestinal ulcers. For the analysis, hazard and risk ratios were used. The results demonstrated no improvement in OS when Y-90 TARE was compared with standard treatments (HR, 0.99; 95% CI, 0.81-1.21; six studies; I^2 = 77.6%). However, Y-90 TARE was correlated with fewer grade ≤ 3 AEs (RR, 0.64; 95% CI, 0.45-0.92; seven studies; I^2 = 66%). No variation was detected in other secondary outcomes. The authors concluded that for the nonsurgical treatment of HCC, Y-90 TARE was not related to a significant effect on OS, PFS, TTP, DCR, and the incidence of gastrointestinal ulcers but showed substantially lower rates of grade ≤ 3 AEs. This systematic review and meta-analysis is limited by the limited number of trials with small numbers of individuals. Well-designed RCTs that compare Y-90 with the standard of care for the nonsurgical treatment of HCC are needed to better define the role of Y-90.

Abdel-Rahman and Elsayed (2020) conducted a systematic review and meta-analysis of six RCTs (n = 1,340) to determine the benefits and harms of Y-90 microsphere radioembolization compared with those of placebo, no intervention, or other available interventions in people with advanced liver cancer. The primary outcomes that were measured were the median OS rate, quality of life, and serious AEs. The secondary outcomes that were measured were cancer-related mortality, TTP of the tumor, and tumor response. One RCT compared radioembolization plus sorafenib vs sorafenib alone in individuals with advanced HCC. The authors found very low-certainty evidence that radioembolization combined with sorafenib might be associated with higher rates of nonserious AEs than sorafenib alone. The median OS was 11.4 months in the sorafenib group and 12.1 months in the radioembolization plus sorafenib group (HR, 1.01; 95% CI, 0.81-1.25; p = 0.95). Two RCTs compared radioembolization vs sorafenib for unresectable HCC in individuals with locally advanced HCC. There was a 1-year mortality rate of 62% in the radioembolization group and 60% in the sorafenib group. The authors found low-certainty evidence that suggests that radioembolization achieved OS and a DCR that was comparable to sorafenib alone. The risk of nonserious AEs was lower with radioembolization. Three RCTs compared radioembolization vs chemoembolization in individuals with intermediate-stage HCC. The 1-year survival was 70% in both groups. The authors found low-certainty evidence that suggests that the risk of serious AEs is similar between

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radioembolization and chemoembolization. (Salem et al., 2016, previously cited in this policy, is included in this systematic review. This study is included in the Comparative Effectiveness Review by Hayes, 2019, updated 2022).

A Hayes Comparative Effectiveness Review compared clinically relevant outcomes following TARE with Y-90 vs outcomes following TACE, drug-eluting bead TACE, and sorafenib in individuals with primary unresectable HCC. Evidence from retrospective comparative studies suggests that Y-90 TARE has comparable efficacy in survival outcomes, potentially superior efficacy in tumor response, and better tolerance compared with TACE in intermediate HCC. Evidence that compared TARE with sorafenib suggests equivalence between the groups in survival and tumor progression outcomes but a potential benefit favoring TARE over sorafenib in tumor response and treatment toxicity. The available evidence regarding the comparison of TARE with drug-eluting bead TACE or comparing TARE with resin (SIR-Spheres®) vs glass microspheres (TheraSphere) is insufficient to permit conclusions regarding comparative effectiveness and safety. An updated literature search was performed on September 30, 2020. One post hoc analysis of an RCT (SARAH), two retrospective cohort studies, four systematic reviews and meta-analyses, one systematic review, and two cost-effectiveness studies were retrieved. The evidence remains insufficient to permit conclusions regarding comparative effectiveness and safety. In the 2022 update, Hayes identified 10 newly published studies, with no change to their current Hayes rating (Hayes, 2019; updated 2022).

Katsanos et al. (2017) conducted a systematic review and network meta-analysis of different embolization options for unresectable HCC. Medical databases were searched for RCTs that evaluated bland TAE, drug-eluting bead TACE, or TARE, either alone or combined with adjuvant chemotherapy, or local liver ablation or external radiotherapy for unresectable HCC up to June 2017. Overall, 55 RCTs that included 5,763 people with preserved liver function and unresectable HCC were included in the evidence review. The authors' review found that all embolization strategies achieved a significant survival gain over control treatment. The estimated median survival was 13.9 months with control, 18.1 months with TACE, 20.6 months with drug-eluting bead TACE, 20.8 months with TAE, 30.1 months with TACE plus external radiotherapy, 33.3 months with TACE plus liver ablation, and 24.3 months with TARE. A comparative safety analysis demonstrated that TARE with a beta emitter was the safest treatment, whereas combined TACE and liver ablation had the most favorable safety and effectiveness profile. TACE, drug-eluting bead TACE, TARE, and adjuvant systemic agents did not improve objective response over bland embolization alone. The authors concluded that TACE, drug-eluting bead TACE, TARE, and adjuvant systemic agents neither improved tumor objective response nor granted any individual survival benefit compared with bland particle embolization TAE. Combinations of TACE with external radiation or liver ablation achieved the best tumor response and survival. The quality of evidence remains mostly low to moderate because of clinical diversity.

Clinical Practice Guidelines

American Association for the Study of Liver Diseases (AASLD)

In a 2025 update to the practice guideline regarding prevention in and diagnosis and treatment of patients with HCC, the AASLD states the following:

- TARE with Y-90 has recently been established as an acceptable treatment for solitary unresectable HCC.
- Neoadjuvant LRT such as with TACE, TARE, ablation, and external beam radiation therapy is typically used as a bridge to control tumor growth and reduce the risk of waitlist dropout. Currently, no one type of LRT is recommended over another for bridging to transplant.
- TARE can be performed for subcapsular tumors in anatomical locations that may be challenging for ablation, such as subdiaphragmatic and pericardiac tumors, and is also effective at treating microsatellites. Radiation segmentectomy can provide durable local tumor control, significantly prolong TTP, and serve as an effective bridging therapy to liver transplant.
- TARE can be used as an accepted alternative intra-arterial therapy for intermediate-stage HCC.

Guidance statements:

- Patients with Barcelona Clinic Liver Cance stage B HCC should be treated with TACE (level 1; strong recommendation).
- Radioembolization as an alternative therapy to chemoembolization in patients with Barcelona Clinic Liver Cance stage B HCC (level 3; strong recommendation).
- Transarterial therapies should be performed in a selective/segmental fashion (over lobar treatment) whenever possible, given a lower risk of hepatic dysfunction (level 5; strong recommendation).

(Heimbach 2017)

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American College of Radiology (ACR)/American Brachytherapy Society (ABS)/American College of Nuclear Medicine (ACNM)/American Society for Radiation Oncology (ASTRO)/ Society of Interventional Radiology (SIR)/Society of Nuclear Medicine and Molecular Imaging (SNMMI)

In a 2019 joint practice parameter, revised in 2024, regarding SIRT or radioembolization for the treatment of liver malignancies, the above professional societies state that SIRT and radioembolization may be indicated in the presence of unresectable or inoperable primary or secondary liver malignancies in patients with a performance status that allows the patient to benefit from the therapy and a life expectancy of at least 3 months. The tumor burden should be liver dominant and not necessarily exclusive to the liver. Multidisciplinary expertise is essential and includes interventional radiology, radiation oncology, nuclear medicine, medical physics, radiation safety, hepatology, gastroenterology, medical or radioembolization oncology, and surgical oncology. Laboratory data should suggest that the procedure can be performed safely.

Absolute contraindications:

- Inability to catheterize the hepatic artery.
- Fulminant liver failure.
- Initial mapping angiography, contrast-enhanced cone-beam CT, and/or technetium-99m macroaggregated albumin hepatic arterial perfusion scintigraphy demonstrating clinically unacceptable nontarget deposition that cannot be ameliorated with embolization or delivery adjustment.
- Pretreatment hepatic arterial administration with technetium-99m macroaggregated albumin demonstrative of unfavorable (or unacceptable) shunt fraction between the liver and the pulmonary parenchyma. This shunt fraction must not be greater than acceptable limits specific to each Y-90 product.
- Acute hepatic infection.
- Uncorrectable coagulopathy.

Relative contraindications:

- Excessive tumor burden in the liver with greater than 50% to 70% of the parenchyma replaced by the tumor. In the setting of more extensive tumor burden, treatment can be considered if synthetic hepatic function is preserved.
- Total bilirubin greater than 2 mg/dL (in the absence of obstructive cause), which indicates severe liver function impairment. Nonobstructive bilirubin elevations may indicate that liver metastases have caused liver impairment to the degree in which risks outweigh the benefits for this therapy. In contrast, patients with HCC and elevated bilirubin may be treated with radioembolization if a segmental or subsegmental infusion can be performed.
- Prior radiation therapy to the liver or upper abdomen that included a significant volume of the liver (clinical judgment by the authorized user required).
- Care must be exercised when patients are on systemic therapies that may potentiate or may alter the impact of radioembolization, and caution should be taken when combining therapies.
- Therapy during pregnancy may possibly be an option in extraordinary circumstances and with multidisciplinary consultation and considerations.

NCCN

The NCCN Guidelines in oncology for HCC state that arterially directed therapies for all tumors, irrespective of location, may be amenable to arterially directed therapies, provided that the arterial blood supply to the tumor may be isolated without excessive nontarget treatment. These therapies include TAE, TACE, drug-eluting bead TACE, and radioembolization with Y-90 microspheres. It is stated further that all arterially directed therapies are relatively contraindicated in patients with bilirubin of > 3 mg/dL, unless segmental treatment can be performed.

National Institute for Health and Care Excellence (NICE)

NICE recommends the use of SIRT SIR-Spheres and SIRT TheraSphere as an option for treating unresectable, advanced HCC in adults. NICE recommends the use of SIRT in adults when used for patients with Child-Pugh grade A liver impairment when conventional transarterial therapies are inappropriate and when the commercial arrangement is used in providing SIR-Spheres and SIRT TheraSpheres. Guidance from NICE states that the current evidence on the safety and efficacy of SIRT for primary HCC is adequate for use with normal arrangements for clinical governance, consent, and audit (NICE, 2021; updated 2024).

American College of Radiology (ACR)

In the 2022 appropriateness criteria for management of liver cancer, the ACR states the following:

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TARE with Y-90 microspheres may be appropriate for the following:

- A cirrhotic solitary tumor less than 3 cm.
- ICC: Peripheral hepatic lobar cholangiocarcinoma less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.
- Ductal cholangiocarcinoma: Hilar cholangiocarcinoma greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.
- Solitary colorectal liver metastasis.
- Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

TARE with Y-90 microspheres is usually appropriate for:

- A cirrhotic solitary tumor of 3 to 5 cm.
- Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
- Cirrhotic, multifocal, bilobar disease, with at least one tumor greater than 5 cm.
- Cirrhotic solitary or multifocal disease with vascular invasion.

Intrahepatic Cholangiocarcinoma

Yu et al. (2024) conducted a retrospective review in 28 consecutive patients with ICC that were treated with SIRT at a single institution to evaluate safety and efficacy. The inclusion criteria were adults with biopsy-proven ICC (regardless of prior treatment), local or locally advanced disease, serum total bilirubin of < 2.0 mg/dL, and serum albumin of > 3 g/dL. Five patients had cirrhosis, ECOG performance status was greater than 0 in 10 patients, three had undergone prior resection, and 82.1% of patients had received prior chemotherapy. A multidisciplinary team, including medical oncologists, abdominal imaging radiologists, vascular and interventional radiologists, pathologists, hepatobiliary surgeons, and transplant surgeons evaluated patients for treatment, resectability, and potential transplant. Surgical options included surgical resection, orthotopic liver transplant, living donor transplant, and ex vivo resection. All SIRT treatments consisted of two separate outpatient procedures, totaling 38 sessions, with additional lobar dose to induce functional liver reserve hypertrophy performed on a case-by-case basis and administered in patients who were undergoing potential resection. All patients received SIRT of Y-90 to the target tumor via a segmental or lobar artery, with the target dose calculated using internal radiation dose schema. Additional sessions were performed to achieve contralateral hypertrophy or as needed based on initial tumor response. The primary outcome was OS. Tumor response was calculated using the RECIST criteria, and toxicity was evaluated based on the CTCAE v5.0. At a median follow-up of 12.1 months, all patients were assessed for OS and radiological response, and the results showed that the post median survival time was 22.9 months, with a 1-year survival rate of 78.4%. Two-year OS was 45.1%. Ten patients who could be staged for surgical intervention had a longer OS. In this group, the 1-year and 2-year OS in patients was 100% and 62.5%, respectively. Radiological response, according to RECIST, showed complete response in three patients, partial response in 13, and stable disease in three. Toxicity results showed one grade 3 and one grade 4 hyperbilirubinemia. Grade 3 anemia and pleural effusion/pleurobiliary fistula were reported individually. The authors concluded that favorable OS and few major AEs suggest that SIRT is effective in maintaining local tumor control and is feasible as an intervention in downstaging for surgical resection and transplant. The sample size was small and limited to a single institution. Multi-institutional studies would strengthen these findings.

Schaarschmidt et al. (2023) conducted a multicenter retrospective study to identify factors associated with an improved median OS in patients with ICC who were receiving radioembolization at five major tertiary care centers. The overall analysis included 138 radioembolizations performed in 128 patients with ICC. The outcomes measured were clinical data, imaging characteristics, radioembolization reports, and data from RECIST 1.1 at 3, 6, and 12 months after radioembolization. The mean OS was then compared with subgroups using the Kaplan-Meier curves and the log-rank test. As a first-line treatment, radioembolization was performed in 25.4% of patients, in 38.4% as a second-line treatment, and in 36.2% as a salvage treatment. In those receiving first-line, second-line, and salvage radioembolization, the DCR was 68.6%, 52.8%, and 54.0% after 3 months; 31.4%, 15.1%, and 12.0% after 6 months; and 17.1%, 5.7%, and 6.0% after 1 year, respectively. In patients who were receiving radioembolization as first-line, second-line, and salvage treatment, mean OS was 12.0 months (95% CI, 7.6-23.4 months), 11.8 months (95% CI, 9.1-16.6 months), and 8.4 months (95% CI, 6.3-12.7 months), respectively. No significant differences among the three groups were observed ($p = 0.15$). Hepatic tumor burden did not significantly influence mean OS ($p = 0.12$). The authors concluded that radioembolization might be an essential treatment option, especially in advanced ICC, as a second-line and salvage treatment. Further research is necessary to investigate the role of radioembolization as a first-line treatment and in the later treatment stages of the disease.

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Chan et al. (2022), in a phase 2, single-arm, multicenter clinical trial, aimed to study the efficacy and safety of administering SIRT with resin Y-90 followed by standard chemotherapy for unresectable ICC. For the study, participants were administered SIRT at a dose of 120 Gy targeted at the tumor and then started gemcitabine 1,000 mg/m² and cisplatin 25 mg/m² on days 1 and 8 of a 21-day cycle. The outcomes measured were OS, PFS, response rate according to RECIST 1.1, toxicity, and time from SIRT to commencement of chemotherapy. Overall, 31 participants were screened, and 24 were recruited; all completed SIRT, although only 16 received chemotherapy. The study results showed that the median cycle of chemotherapy was five (range, 1-8). The median OS was 13.6 months (95% CI, 5.4-21.6 months) in the ITT population. Among 16 participants who were undergoing chemotherapy, the median OS was 21.6 months (95% CI, 7.3-25.2 months), and the median PFS was 9 months (95% CI, 3.2-13.1 months). The response rate was 25% (95% CI, 3.8%-46.2%), and the DCR was 75% (95% CI, 53.8%-96.2%). No new safety signal was observed, with fewer than 10% of participants experiencing a grade 3 or higher treatment-related AE. The median time from SIRT to chemotherapy was 29 days (range, 7-42 days). Eight participants could not receive chemotherapy due to rapidly progressive disease (n = 4), underlying treatment-unrelated comorbidities (n = 2), and withdrawal of consent due to personal reasons (n = 2). The authors concluded that treating SIRT followed by chemotherapy is feasible and effective for unresectable ICC. However, further studies are necessary to determine the optimal sequence of SIRT and chemotherapy. Limitations of the study include a need for more diversity in the population and control arm and the need for analyses on tissue biomarkers relevant to the SIRT-chemotherapy combination.

Schartz et al. (2022) conducted a systematic review and meta-analysis using a random-effects model to assess the use of Y-90 for unresectable ICC. The study evaluated cancer antigen 19-9 response rate, DCR, downstaged to resectable rate, pooled OS, pooled median PFS, and mean reported survival rates between 3 and 36 months. Overall, 921 individuals were included from 21 studies. The outcomes showed that the DCR was 82.3% overall, 11% of those were downstaged to being surgically resectable, and the cancer antigen 19-9 response rate was 67.2%. PFS was 7.8 months from the point of radioembolization, with the overall median survival rate being 12.7 months. The reported survival proportions were at 3, 6, 12, 18, 24, 30, and 36 months. The authors concluded that radioembolization with Y-90 for unresectable ICC remains beneficial for both disease control and survival.

Fruscione et al. (2021) performed a systematic review on neoadjuvant therapy for unresectable ICC and the association with adequate tumor downsizing to enable resectability. Ten studies (n = 132) were included in the review: two retrospective, single-center studies; one retrospective, multicenter study; one prospective study; one prospective safety study; and five case reports. With case reports excluded, 22 of 127 individuals (17.3%) had successful tumor downsizing based on treatment modality. Tumor downsizing rates ranged from 13.9% (TACE alone) to 20.8% (TARE alone). Overall, 27 people underwent conversion therapy with surgical resection. The authors concluded that conversion therapy for initially unresectable ICC may offer adequate tumor downsizing for resection.

White et al. (2019) conducted a prospective observational study to evaluate the outcomes in participants with unresectable, chemotherapy-refractory ICC who were treated with TARE. The primary outcome was OS. The secondary outcomes included safety, PFS, and liver-specific PFS. The study included 61 people; 91% had a performance status of 0/1, 92% had received prior chemotherapy, and 59% had no extrahepatic disease. The median follow-up was 13.9 months (95% CI, 9.6-18.1 months). OS was 8.7 months (95% CI, 5.3-12.1 months), and 37% of participants survived to 12 months. PFS was 2.8 months (95% CI, 2.6-3.1 months), and liver-specific PFS was 3.1 months (95% CI, 1.3-4.8 months). One severe complication (abdominal pain) occurred at the time of the TARE procedure. Overall, 30 participants experienced a total of 49 AEs, of which 8% were grade ≥ 3; the most common were grade 1 to 2. Those with advanced ICC have limited therapeutic options and a poor prognosis. The authors concluded that the results demonstrate that this treatment merits further investigation in this cohort in a larger study, including collection of participant-reported outcomes.

Clinical Practice Guidelines

American College of Radiology (ACR)

In the 2022 appropriateness criteria for the management of liver cancer, the ACR states that TARE may be appropriate for peripheral hepatic lobar cholangiocarcinoma that is less than 3 cm and without biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.

NCCN

The NCCN Guidelines for biliary tract cancers state that LRT is a treatment option that may be considered for patients who are not candidates for curative surgical treatment or to downstage for other treatments. Locoregional therapies include arterially directed therapies, for which the guidelines state the following:

- Therapies include TAE, TACE, TACE with drug-eluting beads, and Y-90.

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- Select patients with limited extrahepatic disease (hilar lymph node ≤ 3 cm or five or fewer lung nodules, each ≤ 1 cm) may be considered for arterially directed therapy in combination with systemic therapy.
- May be used alone or followed by systemic chemotherapy, with the intention of prolonging survival or to downstage for curative resection.
- When treating with Y-90, personalized dosimetry/radiation segmentectomy to achieve > 205 Gy to the tumor may improve the outcome.
- In patients with bilirubin of > 3 mg/dL, Y-90 is a relative contraindication.

National Institute for Health and Care Excellence (NICE)

NICE interventional procedures guidance for SIRT for unresectable primary ICC recommendations states that the current evidence on the safety of SIRT for unresectable primary ICC shows that there are well-recognized, serious but rare safety concerns. Evidence on its efficacy is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research. They recommended that further research in the form of prospective studies, including RCTs, should address patient selection, quality-of-life outcomes, and OS. Patient selection for the research studies should be done by a multidisciplinary team. The procedure should only be done in specialist centers by clinicians who are trained and experienced in managing cholangiocarcinoma (NICE, 2018).

Uveal Melanoma

Alexander et al. (2022) conducted a systematic review to assess the effectiveness and safety of SIRT for hepatic metastases from uveal melanoma (UM). Research from Embase and MEDLINE until July 2020, using terms related to SIRT and hepatic from UM, was used and showed outcomes of SIRT in individuals with UM and one hepatic metastasis. Data were collected on OS, HPFS, and tumor response. The Newcastle-Ottawa Scale assessed the risk of bias. The literature reported outcomes in 268 individuals with hepatic metastases from UM using 11 studies. Overall, 170 individuals achieved disease control, with the median OS from the time of SIRT at 12.3 months. The median HPFS was 5.4 months, with serious complications seen infrequently. Median Newcastle-Ottawa Scale score showed a moderate risk of bias, with a score of 6. Limitations include questionable results due to retrospective data, with a moderate risk of bias.

Rowcroft et al. (2020) conducted a systematic review to assess the evidence on the management of UM liver metastases. The primary outcome was OS, with disease-free survival as a secondary outcome. Overall, 55 studies were included (n = 2,446), with 39 retrospective cohort studies, two RCTs, and 14 prospective cohort studies. Treatment modalities included surgery, isolated hepatic perfusion (IHP), hepatic artery infusion (HAI), TACE, SIRT, and immunoembolization. Ten studies evaluated surgical resection. The median OS ranged from 10 to 35 months. Ten studies used either IHP or percutaneous IHP to treat UM liver metastases, with the median OS ranging from 9 to 25 months. There were eight studies that evaluated the use of HAI, with OS ranging from 10 to 24 months. Overall, 17 studies evaluated the use of TACE. The reported OS ranged from 5 to 29 months. Six studies evaluated the use of SIRT, in which the median OS ranged from 9 to 24 months. Immunoembolization had a median OS of 21 months. The authors concluded that predominantly retrospective and uncontrolled studies suggest that surgery and locoregional techniques may prolong survival. This review is limited by the low quality of evidence available.

Gonsalves et al. (2019) reported the results of a phase 2, two-parallel-arm, prospective trial on the safety and efficacy of radioembolization for treating UM hepatic metastases. Participants were enrolled into one of two study groups. Group A included 23 participants with no prior liver-directed or systemic therapies, and group B included 24 participants with hepatic tumor progression following immunoembolization. The inclusion criteria required confirmed UM hepatic metastases (≥ 1 cm) and an ECOG performance status of less than or equal to 1. Participants underwent unilobar, fractionated, whole-liver or sequential lobar treatments every 3 to 5 weeks. Procedure-related complications were classified using the SIR classification system of complications by outcome. Follow-up included blood tests every week for a month, every 2 weeks for 2 months, and every month afterward. Chest, abdominal, and pelvic CT was performed 1 month following treatment to help detect extrahepatic disease. CT, PET, and MRI were performed every 3 months for surveillance of extrahepatic metastases and tumor response. MRI was performed at 3 months for confirmation of tumor response if there were concerns. Participants were evaluated for 1 month and every 3 months for acute and delayed toxicities, respectively. The results showed that in group A, radiographic partial response was achieved in nine of the 23 participants, stabilization of disease was achieved in 11, and three had disease progression. None had a complete response. The median PFS was 8.1 months, and the median OS was 18.5 months. New disease was detected in all participants with disease progression, and extrahepatic disease developed or progressed in 21 participants at a median of 6.6 months. For group B, the results showed that radiographic partial response was achieved in eight participants, stabilization of disease was achieved in six, and 10 had disease progression. None had a complete response. The median PFS was 5.2 months, and the median OS was 19.2 months. Overall, 21 developed new hepatic lesions, and extrahepatic disease developed in 22. No major treatment-related toxicities occurred in either group. The authors

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concluded that despite the fact that greater than 90% of the participants in this trial developed new hepatic and extrahepatic metastases, prolonged OS was achieved. They concluded that radioembolization is a safe and effective first- or second-line treatment for UM hepatic metastases. This trial is limited by a small sample size.

Clinical Practice Guidelines

NCCN

The NCCN Guidelines on UM state that if disease is confined to the liver, regional therapies such as chemoembolization, radioembolization, or immunoembolization should be considered.

Bridge to Transplant

A Hayes Health Technology Assessment report compared clinically relevant outcomes following TARE with Y-90 with other LRTs or sorafenib in individuals with primary HCC as a bridge to transplant or resection. A total of eight studies met the inclusion criteria. All but two studies compared data retrospectively. The remaining studies consisted of two RCTs. The outcome measures included survival, tumor response, TTP, rate of successful downstaging or bridging, and toxicity and other complications. The assessment reported that Y-90 TARE may confer similar or greater benefits than other LRTs or sorafenib with respect to the efficacy outcomes assessed and that Y-90 TARE is comparable to or better than other LRTs or sorafenib in terms of safety. A 2021 review of literature found one additional study. The small body of low-quality evidence suggests that Y-90 TARE may have similar or better safety and efficacy outcomes than other treatments used to downstage or bridge primary individuals with HCC to transplant or resection (Hayes, 2019; updated 2022).

Gabr et al. (2021) conducted a retrospective cohort study (n = 207) to evaluate the long-term outcomes of liver transplant in patients with HCC who were bridged for transplant and downstaged using Y-90. Long-term outcomes included OS, recurrence-free survival (RFS), disease-specific mortality, and time to recurrence. Overall, 169 patients were bridged, and 38 were downstaged to liver transplant. OS rates at 3, 5, and 10 years were 84%, 77%, and 60%, respectively. Overall, 24 patients developed recurrence, with a median RFS of 120 months. Disease-specific mortality at 3, 5, and 10 years was 6%, 11%, and 16%, respectively. There were no differences in OS/RFS in those who were bridged or downstaged. RFS was higher in people with complete and extensive vs partial tumor necrosis. The authors concluded that Y90 is an effective treatment for HCC in the setting of bridging/downstaging to liver transplant.

Ettore et al. (2017) retrospectively evaluated the efficacy of Y90 radioembolization in patients with HCC for downsizing prior to liver transplant. The study included 143 patients who received a transplant for HCC, and in 22 cases, they were treated with Y90 radioembolization before liver transplant. Three people were treated with Y90 radioembolization within the Milan criteria, and 19 were out of criteria before Y90 radioembolization. Four patients had an increasing Model for End-Stage Liver Disease score between Y90 radioembolization and liver transplant. Alpha-fetoprotein decreased after Y90 radioembolization treatment in all cases. No death was observed in the Y90 radioembolization procedure or at liver transplant. In 78.9% of cases, a successful downstaging was observed, and in 100% of cases, bridging was achieved. From Y90 radioembolization treatment, OS was 43.9 months. From liver transplant, the overall mean survival was 30.2 months, with a disease-free survival of 29.6 months. The authors concluded that Y90 radioembolization is effective for downsizing in individuals with HCC prior to liver transplant. [This study is included in the Health Technology Assessment by Hayes (2022)].

Lau et al. (2011) reviewed the role of SIRT with Y-90 microspheres for HCC. The evidence was limited to cohort studies and comparative studies with historical controls. The authors concluded that Y-90 microspheres are recommended as an option of palliative therapy for large or multifocal HCC without major portal vein invasion or extrahepatic spread. They can also be used for recurrent, unresectable HCC; as a bridging therapy before liver transplant; as a tumor downstaging treatment; and as a curative treatment in individuals with associated comorbidities who have otherwise excisable tumors but are not candidates for surgery.

Clinical Practice Guidelines

NCCN

In the NCCN Guidelines on HCC, SIRT and radioembolization (TARE) with Y-90 microspheres are listed as locoregional therapies for bridge to transplant and are recommended for eligible patients to slow tumor progression and the dropout rate from the transplant waiting list, particularly in areas in which wait times are long.

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Liver Metastases From Other Primary Sites

There is limited evidence that supports treatment with TARE/SIRT using Y-90 microspheres for liver metastases from other primary sites, and additional research is needed to determine the clinical utility and safety of this treatment outside of the previously described indications.

Kuei et al. (2015) conducted a systematic review to evaluate the effects of Y-90 radioembolization on nonconventional liver tumors, including those that were secondary to breast cancer, cholangiocarcinoma, ocular and percutaneous melanoma, pancreatic cancer, renal cell carcinoma, and lung cancer. Overall, 28 studies that contained nonconventional primary sites were included for review. Of the studies on SIRT of nonconventional liver metastases, breast cancer was the most studied. This review found seven exclusively breast cancer liver metastases (BRCLMs) SIRT studies, in addition to three mixed primary studies that provide response data. Response rates were between 18% and 61%, and median OS was between 6.6 and 13.6 months. The authors concluded that although the tumor response with SIRT was encouraging, the influence on survival remained unclear. To validate SIRT as a potential first-line adjuvant to chemotherapy, larger multicenter, randomized controlled studies are needed. Eight ICC-only SIRT studies were analyzed. Y-90 SIRT is considered, at some centers, as a preferred first-line therapy for ICC with low tumor burden. Reasons for this include the benefit of being able to downstage previously unresectable ICC for curative resection. Although median OS data are shorter than those for HAI, Y-90 therapy carries fewer risks, including not having to implant a chemoinfusion port. Four studies have been done on Y-90 SIRT of melanoma liver metastases. Given the hypervascularity and aggressive nature of melanoma liver metastases, treatment with SIRT appears to be a reasonable approach at reducing disease progression. The median OS ranges from 7.6 to 10.1 months. Based on the few small cohort studies, the authors stated that SIRT has been demonstrated to be safe and effective at prolonging survival; however, without further comparative studies, the ideal selection criteria and benefit over other regional therapies remain uncertain. Metastatic pancreatic cancer carries a poor prognosis. Alternative locoregional therapies such as Y-90 SIRT have been investigated as adjuncts for the purpose of slowing disease progression. Two small cohort single-center studies have been published. Although the limited available data make survivability benefits unclear, initial reports are encouraging. Median survival is attributed to a 2- to 4-month improvement over conventional gemcitabine combination therapy alone. Improvement over the new chemotherapy regimen FOLFIRINOX (leucovorin calcium, fluorouracil, irinotecan hydrochloride, oxaliplatin) has yet to be demonstrated. Response rates are consistent with established response rates in colorectal and neuroendocrine metastatic liver disease. Further studies are needed to delineate the proper selection criteria for optimal individual outcome. Experience with locoregional therapies like SIRT in the treatment of renal cell carcinoma liver metastases is very limited. In the treatment of liver metastasis from renal cell carcinoma, SIRT is limited by the rarity of liver-dominant metastases and the known resistance to radiation. Data for a handful of individuals are promising for the use of SIRT for a palliative rather than curative intent. The value of Y-90 SIRT and lung cancer has been seldom investigated, and the available data are extremely limited. The authors concluded that the few cases of Y-90 SIRT of lung cancer liver metastases demonstrate SIRT's potential as an effective salvage therapy. Clinicians must be mindful of nontarget radiation to the lungs due to potentially limited baseline pulmonary function. Further studies are needed so that the criteria for which SIRT becomes a worthwhile therapy in metastatic lung cancer can be better defined. The authors summarized that although the indications for Y-90 SIRT in nonconventional liver metastases are less well defined, the initial results of small studies are largely favorable. Limitations include marked cohort heterogeneity, absence of a gold standard in response criteria, and variations in treatment dosing. These studies demonstrate that whether Y-90 SIRT provides a justifiable benefit to any given person relies tremendously on both tumor type and individual status. Larger, multicentered, randomized controlled studies are needed so that established clinical guidelines can develop that ultimately improve outcomes.

Breast Cancer

Topcuoğlu et al. (2026) conducted a retrospective observational study in 26 women (mean age, 57.9 years) who had progressive disease after first- and second-line chemotherapy for BRCLMs and underwent Y-90 TARE with glass microspheres, primarily as salvage treatment. Patients were excluded if there was a tumor burden of greater than 50% of the liver; a life expectancy of 3 months or less; an ECOG performance status above 2; elevated bilirubin; low albumin; or prior liver-directed therapy. The primary outcomes were OS and HPFS, using the Kaplan-Meier analysis, with fluorodeoxyglucose PET every 12 weeks using the PET Response Criteria in Solid Tumors. The secondary outcomes were ORR and DCR. The results showed that for the primary outcomes, the median OS and HPFS were 6.1 months and 4.2 months, respectively, with PET responders having longer OS than nonresponders (8.3 vs 4.0 months; $p = 0.025$) but no significant difference in HPFS (4.1 vs 2.1 months; $p = 0.210$). A tumor-absorbed dose of at least 145 Gy was associated with improved OS ($p = 0.024$) but not HPFS ($p = 0.398$). No patients were lost to follow-up. The authors concluded that imaging response was modestly correlated with OS, and tumor-absorbed dose may play an important role in determining OS outcomes, suggesting the value of tumor-absorbed dose as a prognostic marker. Limitations of this

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study include a small treatment population and the refractory nature of the cohort, which may hide exact OS and HPFS benefits. Furthermore, more than 80% had extrahepatic disease, which strongly affects OS.

Cuzzocrea et al. (2026) conducted an umbrella review that systematically synthesized evidence from seven systematic reviews, with or without meta-analyses, and evaluated the efficacy and safety of SIRT for liver cancer metastasized in individuals with breast cancer. Eligible reviews assessed ORR, DCR, and OS. Quality was appraised using the AMSTAR (Measurement Tool to Assess Systematic Reviews)-2 tool. Four reviews were rated as low quality and three as moderate quality, and the review followed PRISMA guidelines without protocol registration. For efficacy outcomes, the results were broad and showed ORRs of 36% to 51%, with DCRs of 85% to 88%. OS outcomes were also broad, heterogeneous across the included studies, and ranged from 9.8 to 11.5 months. Safety analyses were inconsistent but showed generally favorable toxicity profiles, with major gastrointestinal complications under 3% and rare severe hepatic events. The authors concluded that SIRT shows encouraging efficacy and acceptable safety in selected individuals with breast cancer and liver metastases and provides liver-specific disease control that can complement systemic therapy and delay subsequent treatment in appropriately chosen cases, with the most favorable outcomes in individuals with liver-only or liver-dominant disease and limited hepatic involvement. There are several limitations to this review, including the substantial heterogeneity across the included studies; lack of prospective, randomized trials; lack of individualized dosimetry for treatment; and inconsistent safety data reporting. These limitations do not allow generalizability of the findings. (Smits et al., 2013, previously cited in this policy, is included in this review.)

Liu et al. (2022) conducted a meta-analysis to assess the efficacy of Y-90 SIRT in treating individuals with breast cancer and hepatic metastasis. Overall, 24 studies, comprising 412 individuals, were included. The results suggest that Y-90 is feasible for treating breast cancer with hepatic metastasis that is recalcitrant to other therapies and showed an overall postembolization median survival time of 9.8 months. Individuals with < 25% hepatic metastatic burden and lack of extrahepatic disease had a better response. The tumor response and tumor control rates were 36% to 49% and 73% to 97%, respectively, which is similar to results shown for primary liver cancer. There were no life-threatening adverse effects reported. This meta-analysis is limited by a heterogeneous population of individuals and disease severity, and additional high-quality studies are needed to determine comparative efficacy with other treatment approaches. (This study is included in the umbrella review by Cuzzocrea et al., 2026.)

Rivera et al. (2021) conducted a systematic review of the literature on the efficacy of liver-directed therapies for breast cancer–related liver metastasis. These therapies include hepatic resection, RFA, transarterial chemotherapy and radioembolization (TACE/TARE), and HAI. There were 51 overall studies included, 10 of which were regarding TARE in 380 total individuals. With regard to TARE, nine of the 10 studies provided RECIST response data, and the evidence shows that of the 380 total individuals, nine had complete response, 143 had a partial response, 139 had the disease stabilize, and 44 had disease progression. Eight studies showed a mean OS of 11.5 months. Three provided 1-year survival data of 34.5% to 86%. The authors concluded that treatment of breast cancer–related liver metastasis using TARE does not show vastly improved survival across all included studies. (This study is included in the umbrella review by Cuzzocrea et al., 2026.)

Feretis and Solodkyy (2020) conducted a systematic review to assess the effect of radioembolization with Y-90 on tumor response and to estimate survival post radioembolization in individuals with unresectable hepatic metastases of breast cancer. Twelve studies (n = 452) were included, with 236 individuals having breast metastases that were not confined to the liver. The duration of the follow-up period post radioembolization ranged from 6 to 15.7 months. DCRs varied from 48% to 100%, with an estimated mean response to TARE of 81%. OS post radioembolization ranged from 3.6 to 20.9 months, with an estimated mean survival of 11.3 months. The authors concluded that TARE with yttrium microspheres has a potentially beneficial role in cases with inoperable liver metastases that are secondary to breast cancer. They stated that the absence of RCTs and the retrospective nature of the studies that were included carried the risk of selection bias. Future randomized trials are needed to compare therapies. (This study is included in the 2021a ECRI report and the umbrella review by Cuzzocrea et al., 2026.)

Fendler et al. (2016) conducted a large single-center study to evaluate the safety, efficacy, and prognostic factors for (90)Y-Yttrium microsphere radioembolization of unresectable liver metastases from breast cancer (BRCLMs). Overall, 81 individuals underwent whole-liver radioembolization by application of SIR-Spheres (Sirtex Medical). After radioembolization, all individuals were monitored for 3 days as inpatients for acute toxicity. Late toxicity was evaluated in all individuals until 12 weeks after the first radioembolization. The primary end point was OS after radioembolization, which was defined as the interval between the date of radioembolization until the last date of contact as censored observation or until disease-related death. The results showed that grade ≥ 3 toxicity based on clinical symptoms, bilirubin, ulcer, pancreatitis, ascites, or radioembolization-induced liver disease occurred in ≤ 10% of individuals. Two individuals eventually died from radioembolization-induced liver disease. Sequential lobar treatment and absence of prior

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angiosuppressive therapy were both associated with a lower rate of serious AEs. Median OS after radioembolization was 35 weeks. The authors concluded that radioembolization for BRCLM shows encouraging local response rates, with low incidence of serious AEs, especially in those with sequential lobar treatment or without prior angiosuppressive therapy. High hepatic tumor burden and liver transaminase levels at baseline indicated poor outcome. The retrospective design of this study may have resulted in false low-toxicity findings arising from underreporting. (This study is included in the meta-analysis by Liu et al., 2022.)

Clinical Practice Guidelines

European School of Oncology (ESO)/European Society for Medical Oncology (ESMO)

There are no randomized data that support the effect of local therapy on survival, and every patient must be informed of this when discussing a potential local therapy technique. Local therapy should only be proposed in very selected cases of good performance status, with limited liver involvement and no extrahepatic lesions, after adequate systemic therapy has demonstrated control of the disease. Currently, there are no data to select the best technique for the individual patient (surgery, stereotactic radiation therapy, intrahepatic chemotherapy, etc.). Prospective RCTs of local therapy for BRCLMs are urgently needed, as the available evidence comes only from case series in highly selected patients.(Cardoso et al., 2017)

NCCN

In the NCCN Guidelines for breast cancer, radioembolization therapies for breast cancer metastases to the liver are not addressed.

Pancreatic Cancer

Blume et al. (2025) conducted a retrospective single-center study that evaluated the safety and efficacy of transarterial therapy for hepatic metastases that were secondary to pancreatic acinar cell carcinoma. This was the largest review of liver-directed therapy for metastatic pancreatic acinar cell carcinoma. Nine patients (mean age, 67 years) with biopsy-confirmed pure or mixed neuroendocrine-pancreatic acinar cell carcinoma, liver-dominant disease, an ECOG performance status of 0 to 2, and bilirubin of < 2.0 mg/dL were included. Treatments comprised 14 hepatic arterial embolization and four TARE sessions, with two patients receiving both modalities. Local tumor PFS and OS were assessed using a Kaplan-Meier analysis in Stata version 17, with OS defined from first therapy to death or last contact and local tumor PFS calculated until progression. Median local tumor PFS was 6.77 months (95% CI, 3.23-26.33 months), assisted local tumor PFS was 22.13 months (95% CI, 3.67-31.93 months), and 1-year OS was 66.67% (95% CI, 28.17%-87.83%). AEs occurred in 27.8% of sessions, which were mostly grade 1, with one grade 3 pulmonary embolism and one grade 5 death due to hepatic abscess and sepsis. Median OS was not reached (95% CI, 0.17 to not reached). Five of the nine patients (55.6%) were alive at the time of data review. One-year OS was 66.67% (95% CI, 28.17%-87.83%), and the rate remained constant 2 and 3 years post treatment. The authors concluded that transarterial therapy provides acceptable local control of pancreatic acinar cell carcinoma liver metastases and demonstrated a safety profile that aligned with that in prior studies. Limitations of this study include a small sample size, retrospective data collection, and heterogeneity of the study population, which included patients with varying disease grades and symptom severity. Furthermore, hepatic artery embolization and transarterial radioemoblization were used, and two patients received both treatments, so a comparative assessment could not be done; this contributes to potential selection bias.

Kayaleh et al. (2020) conducted a retrospective cohort study (n = 26) in a single institution to evaluate the safety, efficacy, and OS rate in patients with liver-dominant, metastatic pancreatic cancer that was treated with TARE with Y-90. The median OS from diagnosis was 33 months, from diagnosis of liver metastasis was 21.8 months, and after TARE treatment with Y-90 was 7 months. The median HPFS was 2.7 months. Mild AEs were reported. Baseline and follow-up imaging was available for 22 of 26 patients. At 3 months, partial response was shown in one patient, stable disease in nine patients, and progressive disease in 12 patients. The authors concluded that TARE with Y-90 glass microspheres is safe and led to a promising increase in OS in patients with liver-dominant, metastatic pancreatic cancer. Limitations of this study include the small number of patients and lack of controls. Larger RCTs are needed to validate these findings.

Clinical Practice Guidelines

NCCN

In the NCCN Guidelines on pancreatic cancer, radioembolization therapies for pancreatic metastases to the liver are not addressed. The guideline does state that in rare circumstances of indolent or oligometastatic disease, patients with pancreatic cancer should be referred to a high-volume center to be evaluated for possible metastasis-directed therapy.

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U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

The FDA has approved two commercial forms of Y-90 microspheres: TheraSphere and SIR-Spheres. SIR-Spheres (Sirtex Medical) are resin Y-90 microspheres and are indicated for the treatment of unresectable, metastatic liver tumors from primary colorectal cancer with adjuvant intrahepatic artery chemotherapy of floxuridine. SIR-Spheres received FDA premarket approval (P990065) on March 5, 2002. Supplemental approvals have been identified for the PMA product code NAW. Additional information is available at: http://www.accessdata.fda.gov/cdrh_docs/pdf/p990065a.pdf. (Accessed May 5, 2026)

TheraSphere (BTG) are glass Y-90 microspheres and are indicated for radiation treatment or as a neoadjuvant to surgery or transplant in individuals with unresectable hepatocellular carcinoma who can have placement of appropriately positioned hepatic arterial catheters. Glass Y-90 microspheres are approved by the FDA under the provisions of a Humanitarian Device Exemption (H980006). Additional information is available at: http://www.accessdata.fda.gov/cdrh_docs/pdf/H980006b.pdf. (Accessed May 5, 2026)

The use of TheraSphere and SIR-Spheres is also regulated by the United States Nuclear Regulatory Commission, which grants a license for the use of these products. Refer to the following guidance for further information: https://www.nrc.gov/docs/ML1535/ML15350A099.pdf. (Accessed May 5, 2026)

On March 17, 2021, the FDA approved TheraSphere (Boston Scientific Corp.) premarket approval for use as SIRT for local tumor control of solitary tumors (1-8 cm in diameter) in individuals with unresectable hepatocellular carcinoma, Child-Pugh score A, cirrhosis, well-compensated liver function, no macrovascular invasion, and good performance status. Additional information is available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P200029. (Accessed May 5, 2026)

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Policy History/Revision Information

Date	Summary of Changes
11/01/2026	**Coverage Rationale** • Revised list of proven and medically necessary indications for Transarterial Radioembolization (TARE)/selective internal radiation therapy (SIRT) using yttrium-90 microspheres; replaced "metastasis from uveal/*ocular* melanoma when confined to the liver" with "metastasis from uveal melanoma when confined to the liver" **Definitions** • Updated definition of "Transarterial Radioembolization (TARE)" **Supporting Information** • Updated *Description of Services*, *Clinical Evidence*, and *References* sections to reflect the most current information • Archived previous policy version 2026T0445BB

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its policies and guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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