



Transarterial Radioembolization for Hepatocellular Carcinoma in Korea: Current Clinical Practices, Facility Requirements, and Patient Selection

간세포암의 방사선 색전술 - 준비사항, 적응증 및 사전검사

Dongho Hyun, MD*

Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

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***Corresponding author**

Dongho Hyun, MD
Department of Radiology,
Samsung Medical Center,
Sungkyunkwan University
School of Medicine,
81 Irwon-ro, Gangnam-gu,
Seoul 06351, Korea.

Tel 82-2-3410-2519

Fax 82-2-3410-0084

E-mail mesentery@naver.com

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Before initiating Yttrium-90 (^{90}Y) radioembolization, both the interventional radiology and nuclear medicine departments must prepare facilities for radionuclide handling, implement appropriate radiation protection and monitoring measures, and ensure that all medical personnel possess the required government-issued certification. According to current guidelines, transarterial radioembolization is recommended as an alternative treatment option for patients with a single hepatocellular carcinoma measuring ≤ 8 cm and classified as stage I, II, or III according to the modified Union for International Cancer Control staging system. However, these indications may be adjusted based on the institution's medical clinical setting and resources. Given the potential for irreversible tissue damage from ^{90}Y , treatment efficacy and safety must be assessed through planning angiography and either planar imaging or SPECT-CT using $^{99\text{m}}\text{Tc}$ -macroaggregated albumin.

Index terms Radioembolization; Planning Angiography; $^{99\text{m}}\text{Tc}$ -MAA; Scintigraphy; Hepatocellular Carcinoma

INTRODUCTION

Hepatocellular carcinoma (HCC) is the sixth most common cancer and the third leading cause of cancer-related mortality worldwide (1). Transarterial radioembolization (TARE) was first included in the Barcelona Clinic Liver Cancer (BCLC) guidelines in 2022 as an alternative treatment option for solitary HCC ≤ 8 cm in diameter (2). In contrast, the Korean Liver Cancer Association–National Cancer Center

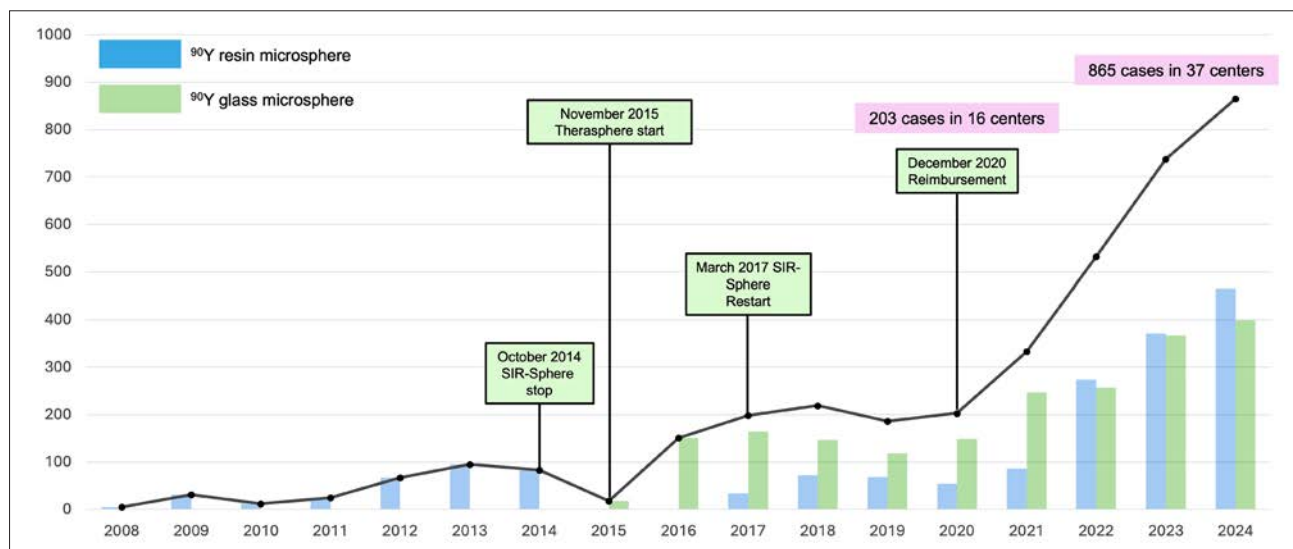
(KLCA-NCC) guidelines recommend TARE as a treatment option across all disease stages (3). In Korea, the use of TARE has sharply increased, although approximately two-thirds of cases are concentrated in a few high-volume centers. Nevertheless, the number of institutions performing TARE continues to grow (Fig. 1). Given these trends, a review of the current national status of TARE in the treatment of HCC is warranted.

FACILITY

Since radioembolization involves both radionuclides and angiographic techniques, close collaboration between the nuclear medicine and interventional radiology departments is required. Technetium-99m (^{99m}Tc) is typically used during planning angiography, while yttrium-90 (^{90}Y) and holmium-161 (^{161}Ho) are primarily employed during the treatment phase (4, 5). However, ^{161}Ho -poly(L-lactic acid) microspheres (QuiremSphere®) are currently not available in Korea. Radionuclides are temporarily stored in the Nuclear Medicine Department and transported to the angiography suite by a registered radiation technician. Unlike ^{90}Y glass microspheres, which are delivered in a vial with a fixed radioactivity, ^{90}Y resin microspheres can be aliquoted into multiple daughter vials on-site within the nuclear medicine department. Details regarding nuclear medicine facilities, such as fume hoods and survey meters, are beyond the scope of this article.

After ^{99m}Tc and ^{90}Y are infused via a microcatheter, both the operators and the angiography suite are surveyed for potential radionuclide contamination. To minimize contamination risk, operators and medical staff wear shoe covers, and a disposable floor cover is draped around the angiographic equipment prior to the procedure (Fig. 2). In accordance with national radiation protection regulations, any angiography suite designated for radioembolization must be registered for radionuclide usage before the procedure. The angiography suite must also comply with legal requirements and be overseen by the institutional radiation safety officer. Beyond standard protection measures, additional shielding for beta radiation from

Fig. 1. The statistics of ^{90}Y transarterial radioembolization in Korea.



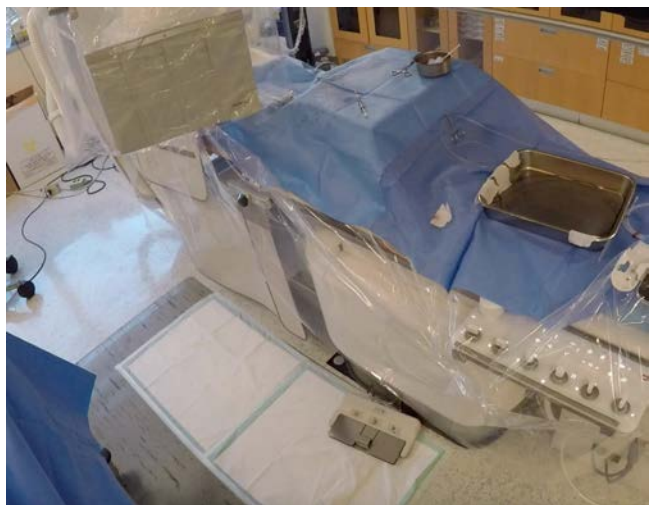


Fig. 2. The disposable floor cover draped around the angioma- chine to minimize possible radionuclide contamination.

Fig. 3. An infusion kit standing on a portable table beside the angioma- chine.



^{90}Y is not required in angiography suites used for TARE. Any personnel involved in TARE—including interventional radiologists, nurses, radiation technicians in both radiology and nuclear medicine departments, and representatives from medical device companies (e.g., ^{90}Y vendors)—are required to hold a government-issued certificate for radionuclide usage, which is renewed annually.

Since $^{99\text{m}}\text{Tc}$ and ^{90}Y emit gamma and pure beta radiations, respectively, appropriate radiation protection measures are implemented for each radionuclide. Basic radionuclide protection principles are applied: time, distance, and protection. For $^{99\text{m}}\text{Tc}$, additional protection such as lead gloves helps reduce gamma ray exposure. In contrast, a plastic infusion kit provides sufficient shielding for ^{90}Y due to its beta emissions. Although some operators wear lead gloves during ^{90}Y infusions, this practice is theoretically ineffective for beta radiation. Infusion kits are supplied by ^{90}Y vendors, and only the Therasphere® infusion kit includes a built-in dosimeter. However, the dosimeter is not intended to measure the absolute radioac-

tivity of ^{90}Y . Multiple infusion kits should be available to accommodate multi-vial use or to replace kits in cases of contamination or operational failure. Additionally, a height-adjustable portable table is prepared to securely support the infusion kit during the procedure (Fig. 3).

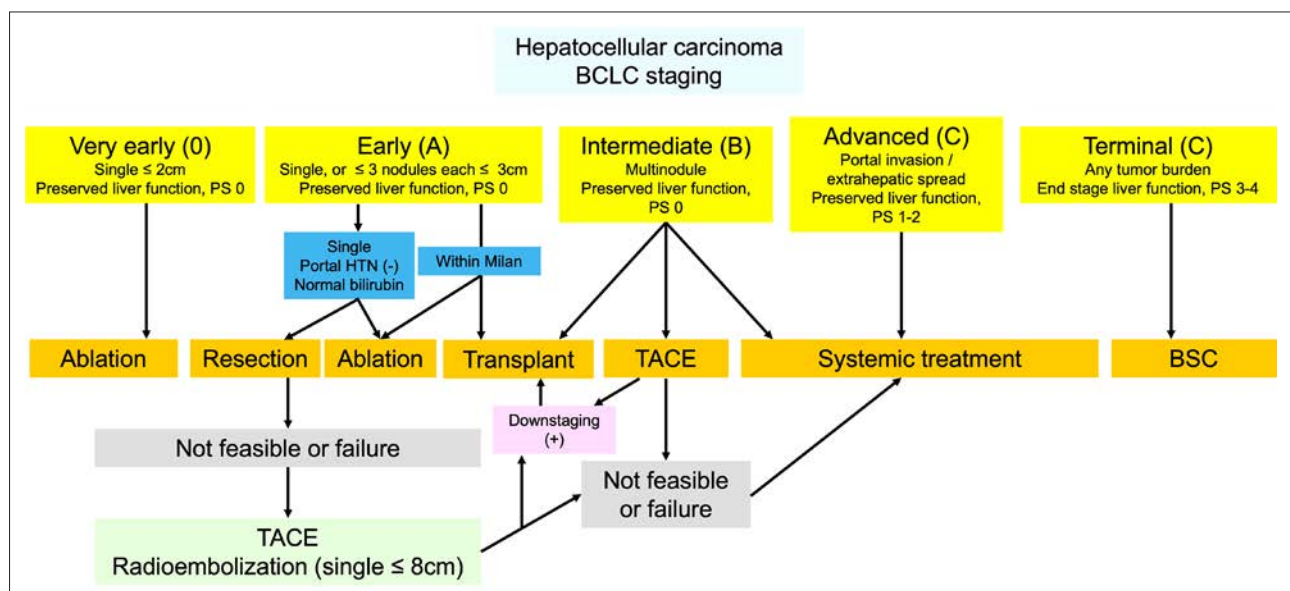
According to the instructions for use (IFU) provided by ^{90}Y vendors, a 2.2-F microcatheter is recommended for both glass and resin ^{90}Y microspheres to minimize the risk of catheter clogging. However, with the growing adoption of radiation segmentectomy and selective delivery techniques, smaller microcatheters, such as 1.98-F and 1.7-F, are increasingly utilized. A Y-rotating valve can be optionally used to facilitate continuous saline flushing and stabilize the microcatheter during the procedure.

PATIENT SELECTION

According to the BCLC staging system, TARE is recommended for patients with solitary HCC ≤ 8 cm in diameter (very early or early stage) when surgical resection, ablation, or liver transplantation is not feasible. Fig. 4 depicts the BCLC staging system and corresponding treatment strategy (2). Evidence supporting this recommendation includes the retrospective multicenter LEGACY study and the prospective single-center RASER study, both of which contributed to the inclusion of TARE as a treatment option (6, 7). The RASER study specifically enrolled patients with HCCs deemed unsuitable for resection or ablation. In both studies, the mean tumor size was <3 cm. Progression-free survival at 2 years was 93.9% in the LEGACY study and 88.0% in the RASER study. The best objective response rate was 88.3% in the LEGACY study, while the RASER study reported an initial objective response rate of 100%. While TARE is often used for downstaging or as a bridging therapy for liver transplantation in the United States, in Korea, it is considered an initial treatment for large, unresectable solitary

Fig. 4. BCLC staging system and corresponding treatment strategy: transarterial radioembolization is one of the alternative treatment options for solitary HCC ≤ 8 cm in diameter when ablation, resection, and transplantation are not feasible.

BCLC = Barcelona Clinic Liver Cancer, BSC = best supportive care, HCC = hepatocellular carcinoma, HTN = hypertension, PS = performance status, TACE = transarterial chemoembolization



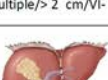
HCC to reduce tumor burden and mitigate the postembolization syndrome associated with conventional transarterial chemoembolization (TACE). However, larger tumors are associated with higher lung shunt fraction (LSF), which can compromise treatment efficacy. Although current BCLC guidelines recommend TACE for intermediate-stage HCC and systemic therapy for advanced-stage HCC, emerging evidence suggests the potential for a paradigm shift. Interim results from the prospective, real-world PROACTIF study reported overall survival rates of 29.6 months for BCLC stage B and 17.7 months for stage C. Furthermore, numerous ongoing studies are investigating the combination of TARE with systemic therapies for patients with BCLC stage C or unresectable HCCs.

According to the KLCA-NCC guidelines, radioembolization may be considered as an alternative treatment option for HCCs in the modified Union for International Cancer Control (mUICC) stages I and II (excluding multiple tumors ≤ 2 cm without vascular invasion), as well as stage III (excluding multiple tumors ≤ 2 cm with vascular invasion). Fig. 5 illustrates the overall treatment strategy (3). TARE is also indicated for patients with localized, multiple HCCs > 2 cm. For cases involving portal vein invasion, TARE may be considered in patients with solitary HCC > 2 cm and Vp1-2 involvement. These national guidelines reflect the current

Fig. 5. First-line treatment recommendations from the 2022 KLCA-NCC Korea practice guidelines for patients with hepatocellular carcinoma who have Child-Pugh class A function, no portal hypertension, and an ECOG performance status of 0–1.

Adapted from Korean Liver Cancer Association (KLCA), National Cancer Center (NCC) Korea. *J Liver Cancer* 2023;23:1-120 (3).

ECOG = Eastern Cooperative Oncology Group, EBRT = external radiotherapy, KLCA-NCC = Korean Liver Cancer Association–National Cancer Center, LT = liver transplantation, RFA = radiofrequency ablation, TACE = transarterial chemoembolization

mUICC stage	Best option (quality of evidence)	Alternative option	mUICC stage	Best option (quality of evidence)	Alternative option
I  Single/ ≤ 2 cm/Vl-	Resection (A) RFA (A)	cTACE TARE Other local ablation EBRT	III  Multiple/ ≤ 2 cm/Vl+	1 st line systemic therapy (A) cTACE+EBRT (B) cTACE (Vp1-2) (B)	
II  Single/ > 2 cm/Vl-	Resection (A) LT (tumor size ≤ 5 cm) (A) RFA (tumor size ≤ 3 cm) (A)	cTACE, TARE DEB-TACE (size > 3 cm) TACE+RFA (size 3-5 cm) Other local ablation (tumor size ≤ 3 cm) EBRT +/- TACE	IVa  Multiple/ > 2 cm/Vl+	1 st line systemic therapy (A) cTACE+EBRT (B)	cTACE HAIC
II  Multiple/ ≤ 2 cm/Vl-	LT (within Milan criteria) (A) cTACE (A) RFA (tumor number ≤ 3) (B)	Resection (tumor number ≤ 3) Other local ablation (tumor number ≤ 3) EBRT (tumor number ≤ 3)	IVa  Node+/no metastasis	1 st line systemic therapy (A)	Systemic therapy + TACE Systemic therapy + EBRT
II  Single/ ≤ 2 cm/Vl+	cTACE (B) cTACE+EBRT (B) 1 st line systemic therapy (Vp3-4) (A)	Resection TARE EBRT	IVb  Metastasis+	1 st line systemic therapy (A)	Systemic therapy + TACE Systemic therapy + EBRT
III  Multiple/ > 2 cm/Vl-	cTACE (A) LT (within Milan criteria) (A) RFA (tumor number ≤ 3 and size ≤ 3 cm) (B)	Resection (tumor number ≤ 3) TARE (localized tumor) EBRT (tumor number ≤ 3 and size ≤ 3 cm) Other local ablation (tumor number ≤ 3 and size ≤ 3 cm)			
III  Single/ > 2 cm/Vl+	1 st line systemic therapy (A) cTACE+EBRT (B) cTACE (B)	Resection EBRT TARE (Vp1-2)			

clinical practice in Korea and are expected to be updated in early 2026. Under current Korean reimbursement policies, TARE is covered for all liver malignancies without limitations on the number of treatment sessions, with 50% of the cost reimbursed. These reimbursement policies are scheduled for revision at the end of 2025.

While various clinical guidelines define the application of TARE based on tumor stage, practice guidelines for personalized dosimetry classify its application into five clinical scenarios: radiation segmentectomy, radiation lobectomy, multifocal unilobar disease, multifocal bilobar disease, and HCC with microvascular invasion and/or portal vein tumor thrombus (PVTT) (Table 1) (8, 9). In cases of portal vein invasion, TARE may be conditionally indicated if ^{99m}Tc -macroaggregated albumin (MAA) is detected within the PVTT on SPECT-CT. This reflects the classification of radioembolization as a transarterial treatment modality, akin to TACE, but utilizing ^{90}Y instead of chemotherapeutic agents. Therefore, indications for ^{90}Y radioembolization may vary between institutions, depending on multidisciplinary assessment and specific clinical practices.

As ^{90}Y is more potent than chemotherapeutic agents such as idarubicin, cisplatin, or doxorubicin and can lead to irreversible damage to the liver parenchyma, baseline liver function, the anticipated future liver remnant volume following TARE, and patient performance status must be carefully evaluated during the initial stages of patient selection. According to the IFU for ^{90}Y , TARE is not recommended when aspartate aminotransferase or alanine aminotransferase levels are >5 times the institutional upper limits of normal, total bilirubin level is >2.5 mg/dL, tumor involvement exceeds 50% of total liver volume as assessed by dynamic CT or MRI, expected perfused liver volume is >70%, or liver cirrhosis is decompensated (Child-Pugh class B with score >7). The guidelines recommend assessing ideal liver function based on specific clinical scenarios (9). A performance status of ≥ 3 on the Eastern Cooperative Oncology Group (ECOG) scale is considered a high-risk factor for liver injury and other morbidities following ^{90}Y radioembolization (8, 10). Treatment-related safety is also considered from the onset and will be further discussed in the next section.

PLANNING ANGIOGRAPHY AND ^{99m}Tc -MAA SCAN

Planning angiography and ^{99m}Tc -MAA scans are essential steps to evaluate the efficacy and safety of radioembolization. During planning angiography, ^{99m}Tc -MAA is infused by an inter-

Table 1. Clinical Scenarios for Considering ^{90}Y Radioembolization

Clinical Scenarios	Treatment Goals	Liver Function (Child-Pugh)	Dosimetry
Radiation segmentectomy	Curative	<B7	Single compartment
Radiation lobectomy	Contralateral hypertrophy, potentially curative	A	Multicompartment
Multifocal unilobar	Palliative	<B7	Multicompartment
Multifocal bilobar	Palliative	A	Multicompartment
HCC with *PVTT and/or microvascular invasion	Palliative	A	Multicompartment

*Good ^{99m}Tc -macroaggregated albumin uptake on SPECT-CT.

HCC = hepatocellular carcinoma, PVTT = portal vein tumor thrombus

ventional radiologist in the angiography suite. This tracer serves as a surrogate for ^{90}Y microspheres used in ^{90}Y radioembolization. Similarly, ^{166}Ho -microspheres are used for ^{166}Ho -based radioembolization procedures. Following tracer infusion, the patient is transferred to the nuclear medicine department for MAA scan, which may include planar scintigraphy or SPECT-CT. Traditionally, the patient is discharged after the scan and re-admitted for ^{90}Y radioembolization if both angiographic and nuclear imaging findings are favorable. However, some centers perform TARE immediately after MAA scan to reduce hospital stay. While radioembolization without a preceding MAA scan—known as streamlining radioembolization—has been attempted, it is not recommended due to safety concerns (11).

From a treatment efficacy perspective, planning angiography aims to delineate the hepatic arterial anatomy, identify hepatic and extrahepatic tumor feeders, and determine the optimal angiographic site for ^{90}Y infusion. Tumor feeders can be visualized in detail using cone beam CT (CBCT) angiography, in addition to digital subtraction angiography (DSA). CBCT is also useful for estimating perfused liver and tumor volumes, which are essential for dosimetry. When multiple ^{90}Y infusions are anticipated, multiple CBCT acquisitions are ideally required. DSA and fluoroscopic imaging are also useful in identifying regions of preferential hepatic arterial blood flow, which may indicate optimal injection sites for ^{90}Y delivery.

Once a microcatheter—typically a 1.98-F catheter—is properly positioned, 5 mCi of $^{99\text{m}}\text{Tc}$ -MAA suspended in normal saline is injected over approximately 20 seconds. The total injection volume is institution-dependent and may vary. Regarding the preparation of $^{99\text{m}}\text{Tc}$ -MAA, a lock syringe is preferred to prevent any leakage between the microcatheter hub and syringe. Both $^{99\text{m}}\text{Tc}$ -MAA and ^{90}Y must be treated as sealed radioactive sources throughout the procedure. Consequently, splitting the $^{99\text{m}}\text{Tc}$ -MAA into daughter syringes within the angiography suite is discouraged. Instead, a nuclear medicine technologist should prepare daughter syringes in advance, with dosing based on the volume of the perfused portion of the liver. A $^{99\text{m}}\text{Tc}$ -MAA scan should be performed promptly following $^{99\text{m}}\text{Tc}$ -MAA infusion, as in vivo biodegradation of $^{99\text{m}}\text{Tc}$ -MAA over time releases free $^{99\text{m}}\text{Tc}$ -pertechnetate. This free tracer can accumulate in various extrahepatic organs, including the stomach, increasing background activity and reducing the accuracy of LSF estimation. For accurate interpretation of the scan, the exact site of radiotracer injection must be communicated to the nuclear medicine physician.

From a safety perspective, the primary purpose of planning angiography is to identify arteries that originate near the hepatic arteries and supply either the extrahepatic organs or normal liver parenchyma. Examples of such arteries include the accessory left gastric artery, cystic artery, umbilical artery, and supraduodenal/retroduodenal arteries. When these arteries are identified, protective measures should be implemented either during planning angiography or before ^{90}Y infusion during the treatment session. These measures may include permanent or temporary coil embolization, the use of quick soluble gelfoam particles, or application of anti-reflux catheters. Although evidence regarding ^{90}Y infusion through extrahepatic feeders is increasing, its safety has not been fully validated (12-14). Consequently, clinical approaches vary. Some operators prefer flow redistribution by embolizing the extrahepatic feeders, while others proceed with ^{90}Y infusion without embolization.

The clinical importance of MAA scan has grown significantly with the advent of personalized dosimetry. In the era of standard dosimetry, planar scan was sufficient for calculating

LSF, determining tumor-to-normal liver (T/N) ratio, and detecting extrahepatic uptake of ^{99m}Tc -MAA. For LSF calculation, regions of interest are drawn around both lungs and the liver. The estimated LSF is calculated by the ratio of counts in both lungs to counts in both lungs and liver, multiplied by 100 (5).

$$\text{LSF} = \frac{\text{Counts (lungs)}}{\text{Counts (lungs)} + \text{Counts (liver)}} \times 100$$

When the LSF is not explicitly reported by the nuclear medicine physician, it can be estimated using dosimetry software. The use of SPECT-CT imaging enhances accuracy in evaluating LSF and identifying extrahepatic uptake, including involvement of non-target organs (15, 16). Moreover, the presence of ^{99m}Tc -MAA uptake in PVTT should be assessed when considering TARE for HCC with vascular invasion (8). Commercially available dosimetry software (e.g., Simplicity^{90Y}™, Boston Scientific) integrates CT or MRI with SPECT-CT data to perform multisegmental dosimetry. However, in Korea, SPECT-CT imaging is not always available in every institution due to limited hardware resources, and the use of dosimetry software is not reimbursed, which presents challenges to implementing advanced dosimetric approaches in clinical practice.

CONCLUSION

Although TARE requires more medical resources than TACE and necessitates collaboration between the interventional radiology and nuclear medicine departments, its role in HCC management is expanding. Rather than strictly adhering to current guidelines, radioembolization should be considered a viable transarterial treatment option. As clinical guidelines continue to evolve, the indications for TARE can be adapted to the medical resources and expertise available at individual institutions. Given that ^{90}Y emits higher energy than conventional chemotherapeutic agents, its efficacy and safety must be evaluated before radioembolization using planning angiography and ^{99m}Tc -MAA scan. The authors hope that this article will help future readers in understanding and preparing for TARE.

Supplementary Materials

Korean translation of this article is available with the Online-only Data Supplement at <https://doi.org/10.3348/jksr.2025.0049>.

Conflicts of Interest

The author has no potential conflicts of interest to disclose.

ORCID iD

Dongho Hyun  <https://orcid.org/0000-0002-2654-7202>

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간세포암의 방사선 색전술 - 준비사항, 적응증 및 사전검사

현동호*

^{90}Y 방사선 색전술을 하기 위해서 인터벤션 영상의학과 의사 및 핵의학과 의료진은 핵종 취급, 방사선 방호 및 검출 조치와 관련된 인적, 물적 시설을 준비해야 한다. 또한 시술 참여 의료진은 방사선작업종사자 교육을 이수 후 매년 갱신해야 한다. Barcelona Clinic Liver Cancer 간세포암 치료 가이드라인에 따르면, 방사선 색전술은 8 cm 이하의 단일 종괴 및 modified Union for International Cancer Control I, II, III 병기에 해당하는 경우 대체 치료 옵션으로 권장되고 있으나 그 적응증은 개별 의료 기관의 의료 환경에 따라 상이할 수 있다. ^{90}Y 는 간조직 및 간외 장기에 비가역적인 손상을 초래할 수 있으므로, 혈관조영술과 $^{99\text{m}}\text{Tc}$ -macroaggregated albumin의 평면 스캔 또는 SPECT-CT를 시행하여 방사선 색전술의 효과 및 안전성을 시술 전에 사전검사를 통해 평가해야 한다.

성균관대학교 의과대학 영상의학교실