

TRANSARTERIAL RADIOEMBOLIZATION (TARE): A PRECISION APPROACH TO LIVER CANCER THERAPY

Hepatocellular carcinoma (HCC) is the 3rd leading cause of cancer death worldwide with approximately 900,000 new cases and 830,000 deaths reported annually.¹ Furthermore, every year, about one third patients with colorectal cancer present with or subsequently develop liver metastases.^{2,3} Curative treatment options including surgery (tumor resection or liver transplantation) or locoregional therapies such as ablation are reserved for early-stage disease. However, for advanced and metastatic disease, systemic therapy is usually used for widespread metastatic disease at the expense of relatively high complication rate. There has been an ongoing effort to develop more effective and less toxic locoregional treatment approaches for patients with oligometastatic disease, including transarterial chemoembolization (TACE) and transarterial radioembolization (TARE).³ These therapies are focused on preventing local progress and cannot systemically control tumor growth.

Transarterial Radioembolization (TARE), also widely known as Selective Internal Radiation Therapy (SIRT), is a sophisticated, minimally invasive procedure used primarily to treat primary and metastatic liver cancers. By leveraging the liver's unique dual blood supply, TARE delivers high-dose targeted radiation directly to malignant tissues while preserving healthy liver function. According to the Barcelona Clinic Liver Cancer (BCLC) staging system, TARE is recommended for patients with solitary HCC \leq 8 cm in diameter (very early or early stage) when surgical resection, ablation, or liver transplantation is not feasible. 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.^{4,5} 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 LEGACY study and 88.0% in the RASER study.^{4,5}

Mechanism of Action: The fundamental principle of TARE is "microembolization" rather than the "macrovascular" ischemia seen in other therapies like TACE.

- **Dual Blood Supply:** Liver has dual blood supply and receives approximately 75% of its blood from the portal vein and 25% from hepatic artery. But hepatic tumors draw nearly 90% of their supply from the hepatic artery.
- **Microsphere Delivery:** Using a catheter in tumor-feeding hepatic artery, millions of tiny radioactive beads (Yttrium-90; Yt-90) are deployed in tumor microvasculature.
- **Local Brachytherapy:** These spheres, ranging from 20 to 60 micrometers, lodge in pre-capillary arterioles within the tumor. They emit beta radiation with a mean tissue penetration of 2.5 mm, causing lethal DNA damage to tumor cells with minimal impact on distant healthy tissue.

Essential Steps: TARE is typically a two-stage procedure. First, a mapping procedure is performed using ^{99m}Tc-MAA (macro-aggregated albumin) injected into the tumor feeding hepatic artery in the catheterization laboratory. This is to simulate the distribution of the radioactive beads and check for "lung shunting" or unintended flow to the gastrointestinal tract in images acquired under gamma camera. The second stage is the actual administration of the Yt-90 labeled microspheres in catheterization suite.

Currently two types of microspheres are commercially available:

1. *Glass Microspheres (Thera-Sphere)*: Feature higher radioactivity per sphere, resulting in less embolic effect and higher localized dose.

2. *Resin Microspheres (SIR-Spheres)*: Feature lower activity per sphere, meaning more spheres are required, which can provide greater embolic effect for larger lesions.

Therapeutic Applications:

Over last few years, several critical roles of TARE have evolved:

- a. Palliative Care: Extending survival and maintaining quality of life for patients with unresectable HCC or cholangiocarcinoma;
- b. Downstaging for Surgery: Shrinking tumors to a size that allows for surgical resection or liver transplantation;
- c. Radiation Lobectomy: Treating a diseased lobe to induce hypertrophy in the healthy lobe and proceed for surgical resection.

Selection criteria for TARE

Eligible patients must have an unresectable, liver-dominant tumors (HCC, NETs, or metastases), ECOG performance status 0–2, and adequate liver function (Child-Pugh A & B; bilirubin <2 mg/dL, albumin >3 g/dL). Ideal candidates have <70% liver tumor bulk, expected survival >3 months, and no severe extrahepatic disease. Patent portal vein is preferred, though TARE can be used with portal vein thrombosis (unlike TACE).

Contraindications of TARE

1. Compromised Liver function (bilirubin >2mg/dL)
2. Extensive extrahepatic disease or poor overall prognosis.
3. Uncorrectable flow to the gastrointestinal tract.
4. Renal failure (creatinine \geq 2 mg/dL or GFR <30 mL/min)

Complications of TARE

TARE is generally well-tolerated procedure and Post-Radioembolization Syndrome is characterized by fatigue, nausea, and abdominal pain. Less common but more severe complications include Radioembolization-Induced Liver Disease (REILD) or radiation pneumonitis due to significant lung shunting (radioembolization of pulmonary microvasculature resulting in radiation dose to Lung >30 Gy). A Lung Shunt Fraction (LSF) >20% (for resin) may require a reduced dosage to avoid radiation pneumonitis.

Role of Imaging in TARE:

Imaging plays a paramount role throughout the TARE continuum - from initial mapping and dose calculation to assessing response and managing complications.⁷ In Pre-Treatment Mapping and Simulation angiography and cone-beam CT is performed to identify tumor-feeding arteries and to look for non-target vessels supplying stomach or gall bladder. Intra-arterial Tc-99m MAA administration is done to simulate microsphere distribution and lung shunt fraction is calculated as LSF >20% (for resin sphere) and lung dose >30 Gy (for glass sphere) may prevent or need dose modification to prevent radiation pneumonitis. For precise dosimetry, CT and MRI are used to measure volume of tumor and targeted liver segment. After the intraarterial administration of Yt-90 microsphere, Bremsstrahlung SPECT-CT and Yt-90 PET/CT are used to document actual intratumoral accumulation and potential

extrahepatic deposition of spheres.⁸ Similarly CT and/or MRI are used for monitoring response assessment at 1 month as baseline followed by 3 months and then every 3-6 months.

Survival Benefit of TARE

Progression-free survival (PFS) after TARE using Yttrium-90-labelled spheres for liver tumors generally ranges from 5 to 10 months, heavily depending on tumor type, stage, and treatment intent (bridging vs. palliative). For HCC, median PFS is often around 7.3 to 9.1 months, with some studies showing superior outcomes when used as a bridge to transplant.^{4,5}

Conflict of Interest: None

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