

Locoregional Therapies Beyond the Liver: Emerging Applications in Extrahepatic Malignancies



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Introduction

- Locoregional therapies (LRTs) have transformed the management of hepatocellular carcinoma (HCC) by providing minimally invasive, targeted tumor control.
- While their role in hepatic malignancies is well established, evidence is emerging for potential applications in extrahepatic disease.¹
- These approaches may offer new treatment avenues for patients with unresectable or refractory tumors without systemic therapy options.¹
- This exhibit reviews current investigational uses of transarterial radioembolization (TARE) and transarterial chemoembolization (TACE) beyond the liver, highlighting their technical and clinical challenges and the future directions needed for integration into standard of care.

Clinical Rationale

- Extrahepatic applications of TARE and TACE remain largely investigational.¹
- Patients with unresectable or refractory extrahepatic tumors often face a therapeutic gap, especially once systemic or surgical options are exhausted or contraindicated.
- Locoregional therapies such as TACE and TARE allow high selectivity of tumors, maintaining chemotoxicity locally rather than systemically.

Translational Significance

- Curative Intent – Investigational usage aims for tumor elimination and disease remission.
- Palliative/Salvage benefit – Reduce tumor burden and reduce symptoms in untreatable cases.
- Tumor biology – More insight into tumor responses and vascular supply across organs.
- Expansion of IR – More opportunities for new oncology interventions.

Growing Applications in Locoregional Therapy

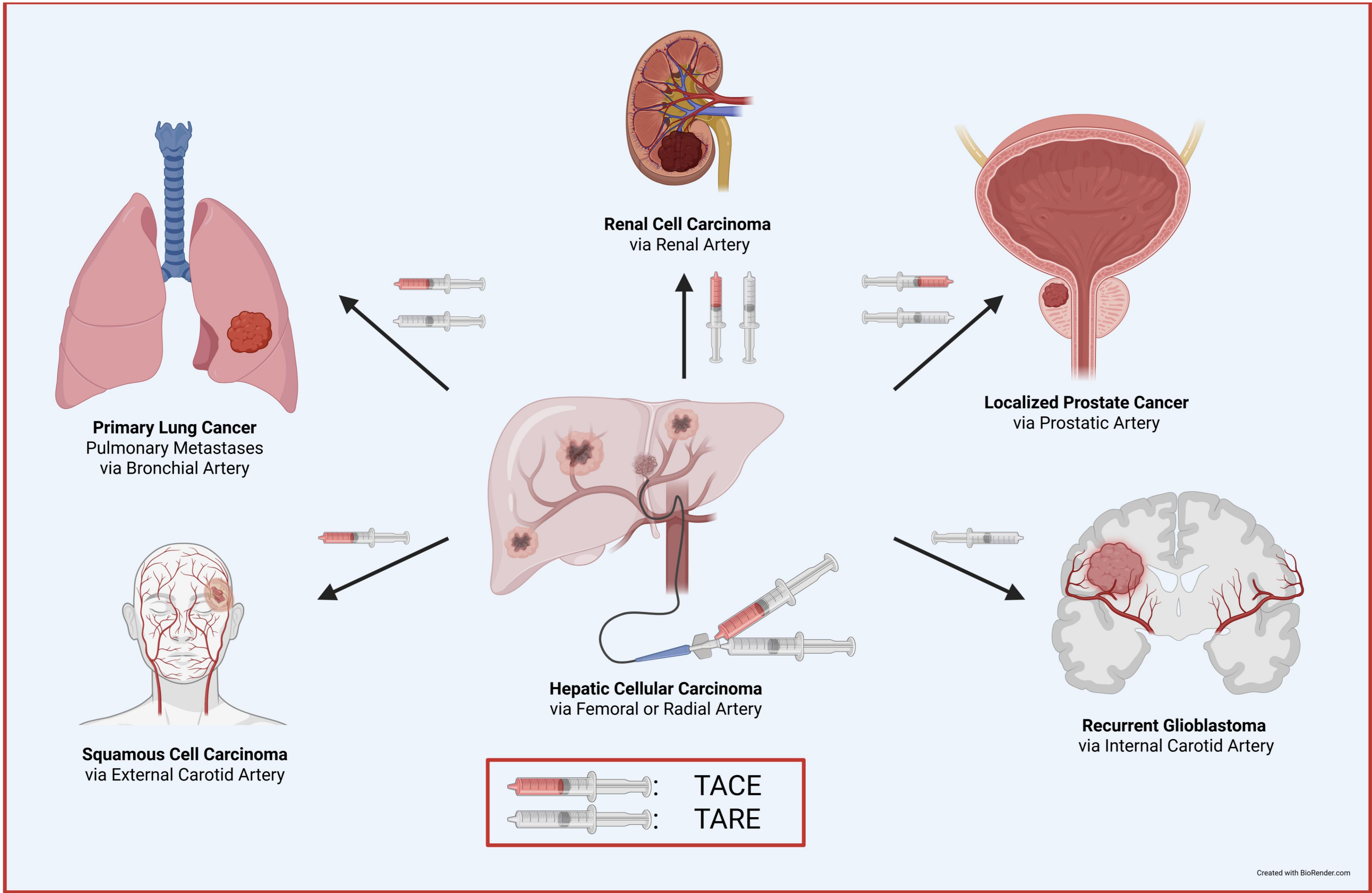


Figure 1: Overview of extrahepatic applications of transarterial chemoembolization (TACE) and transarterial radioembolization (TARE), showing emerging targets in brain, lung, prostate, kidney, and head & neck, with access routes indicated.

Organ of Interest	Cancer Type	Evidence Status
Brain	Glioblastoma (GBM)	FRONTIER Trial (Phase I – <i>in progress</i>) ²
Head/Neck Skin	Squamous Cell Carcinoma (SCC)	Case Reports (TACE) ³
Lung	Non-Small Cell Lung Cancer (NSCLC)	TARE: NCT04105283 (Phase I- <i>completed</i>) ⁴ TACE: NCT04200417 (Phase I – <i>completed</i>) ⁵ , NCT05672108 Phase II – <i>ongoing</i> ⁶
Kidney	Renal Cell Carcinoma (RCC)	TARE: RESIRT Trial (Phase I – <i>completed</i>) ⁷ , RENEGADE Trial (Phase I/II- <i>in progress</i>) ⁸ , ARRC Trial (Phase II- <i>in progress</i>) ⁹ TACE: Retrospective Study ¹⁰
Prostate Gland	Localized Prostate Cancer	TACE: Prospective Study ¹¹ TARE: VOYAGER Trial (Phase I – <i>in progress</i>) ¹²

Figure 2: Overview of current evidence for TACE and TARE in extrahepatic malignancies. Organ sites, associated cancer types, and the levels of supporting evidence to date (case reports, clinical trials) are included.

Results

- Glioblastoma (TARE)²**
 - Preliminary trial data shows toleration and technical success.
 - Challenge: complex vasculature, blood brain barrier, unknown dosimetry, radiation necrosis.
- Head/Neck Squamous Cell Carcinoma (TACE)³**
 - Shown only in case reports with feeding branches from the external carotid for unresectable, recurrent, or bleeding SCC.
 - Challenge: Limited to highly vascular tumors with easy access.
- Lung (TARE/TACE)^{4,5,6}**
 - 1st trial data shows safety/feasibility. Currently assessing efficacy.
 - Challenge: Dual blood supply, radiation pneumonitis.
- Renal Cell Carcinoma (TARE/TACE)^{7,8,9,10}**
 - Retrospective studies and phase I trials report success.
 - Challenges: Organ tolerance threshold, risk to renal function.
- Prostate Cancer (TACE/TARE)^{11,12}**
 - TACE: Prospective study shows safety/feasibility. TARE: First-in-human study.
 - Challenges: Small, variable artery supply; unknown dosimetry, non-target risk.

Discussion

- The extrahepatic usage of TACE and TARE is limited to case reports or preclinical investigations; there are no large trials or consensus guidelines that support their usage.
- Most current efforts are directed towards safety/feasibility or dose-finding rather than efficacy. Organ tolerance dominates safety concerns in critical organs such as the brain and kidneys.
- While current evidence is preliminary, the growing body of prospective data and trial activity shows promise to expand TACE and TARE into novel indications, reshaping non-hepatic oncologic care.

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