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Review Article

# Selective Balloon-occluded Transarterial Chemoembolization for Hepatocellular Carcinoma: Mechanisms, Applications, and Challenges

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## Abstract

Balloon-occluded transarterial chemoembolization (B-TACE) has emerged as a significant advancement in the locoregional treatment of hepatocellular carcinoma. This technique utilizes a balloon microcatheter selectively placed in target hepatic arteries to occlude blood flow and enhance drug accumulation within tumors while minimizing systemic exposure. The feasibility, safety, and effectiveness of the balloon occlusion technique have been verified. Recent studies have demonstrated that B-TACE achieves superior tumor response rates and potentially improves survival outcomes compared with conventional transarterial chemoembolization (C-TACE) techniques, particularly in cases with complex tumor vasculature or C-TACE-refractory disease. However, determining which patients would benefit from B-TACE requires comprehensive assessment. It remains to be determined in clinical practice whether this technique increases the risk of liver function impairment or is associated with specific complications. Further research is needed to better understand the technical conditions required for its clinical application, prognostic factors, and how it can be combined with other interventional techniques. This review summarizes the current literature on B-TACE, focusing on its technical principles, clinical efficacy, safety profile, and evolving role within the contemporary treatment landscape for advanced hepatocellular carcinoma, including its integration with systemic therapies.

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## Introduction

Hepatocellular carcinoma (HCC) is a major global health challenge that ranks as the sixth most common cancer worldwide and the third leading cause of cancer-related mortality.[1] Approximately 900,000 new cases are diagnosed annually, and its incidence continues to increase. Unfortunately, many patients present with advanced disease at diagnosis, which precludes curative interventions such as surgical resection or ablation. Transarterial chemoembolization (TACE) has long been the standard of care for individuals with unresectable HCC, particularly those with intermediate-stage (Barcelona Clinic Liver Cancer stage B) disease.[2]

TACE is the primary treatment method for intermediate-stage liver cancer. Traditional TACE techniques, including conventional TACE (C-TACE) and drug-eluting bead TACE (DEB-TACE), combine localized chemotherapy delivery with arterial embolization to induce tumor necrosis.[3,4] Although effective, these approaches have limitations, including variable drug distribution and suboptimal outcomes in certain patient subgroups, particularly those with a high tumor burden or complex vascular supply. Selective balloon-occluded TACE (B-TACE) addresses several of these limitations through enhanced vascular control and improved drug delivery kinetics.[5–7]

Several technical refinements have been made to enhance the efficacy of TACE. In 2009, Irie *et al*.[8] first reported that B-TACE improves lipiodol deposition by occluding the proximal vessel with a microballoon catheter during selective TACE, thereby preventing backflow of the embolic material. By inflating a microballoon catheter in the tumor-feeding artery to alter local hemodynamics, the procedure aims to enhance tumor saturation with embolic agents and drugs while preventing non-target embolization. Following its initial application in C-TACE,[9] this technique has been progressively adopted for DEB-TACE and selective internal radiotherapy (SIRT).[10,11] Despite the absence of definitive indications for B-TACE to date, several studies have explored its clinical efficacy and related prognostic factors, warranting further clinical attention.

Previous reviews on B-TACE for HCC are largely narrative, technically focused, or outdated, lacking systematic comparisons across TACE modalities and critical appraisal of recent evidence. This review addresses these gaps by providing an updated synthesis that covers hemodynamic mechanisms, comparative efficacy and safety, patient selection, complications, and future combination strategies, along with a critical assessment of evidence quality. To our knowledge, this is the first review to systematically com-

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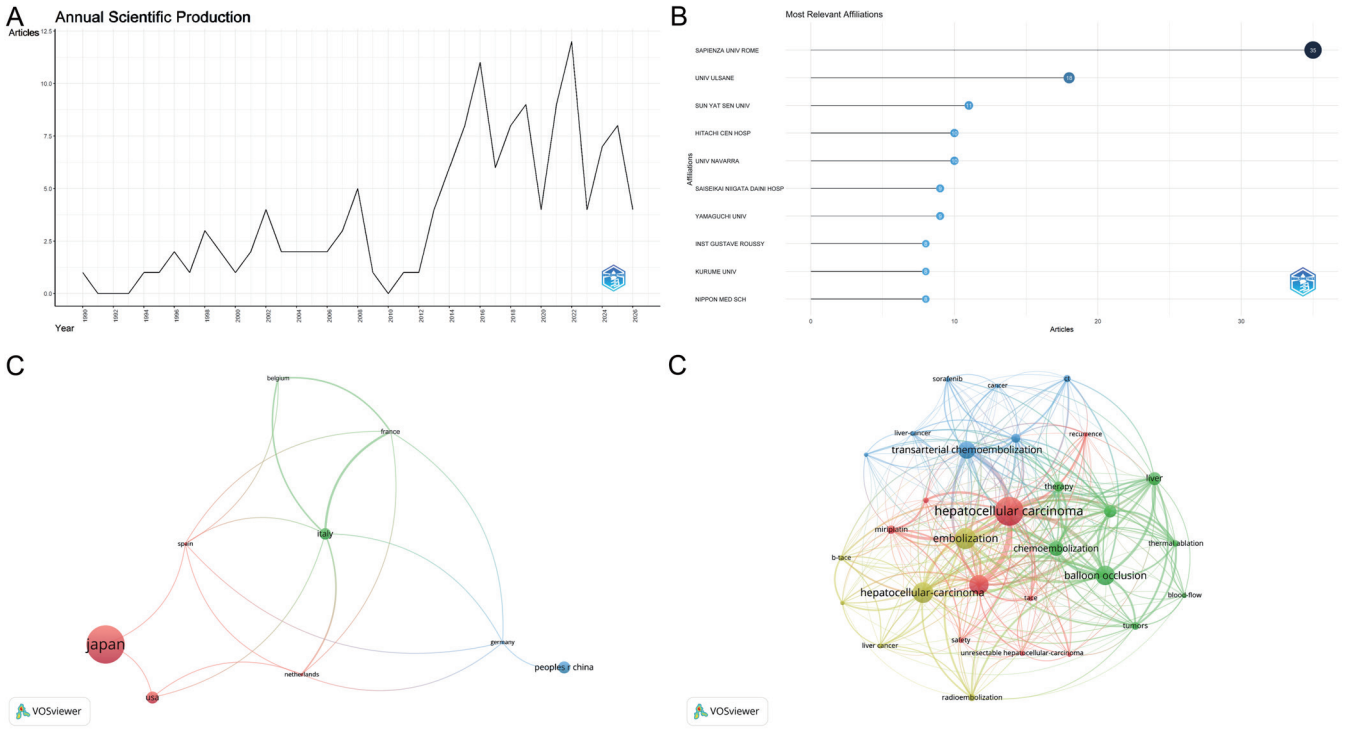


**Fig. 1. Bibliometric overview of B-TACE research.** (A) Annual scientific production. (B) Most relevant affiliations. (C) Country collaboration network. (D) Keyword co-occurrence map. B-TACE, balloon-occluded transarterial chemoembolization.

pare B-TACE with other TACE modalities while incorporating the latest evidence.

## Bibliometric analysis of B-TACE research

To provide an overview of the research landscape and development trends of B-TACE for HCC, a bibliometric analysis was conducted. Relevant publications were retrieved from the Web of Science Core Collection (WoSCC) database from database inception to 2026. The following search strategy was applied: TS = (("hepatocellular carcinoma" OR HCC OR "liver cancer") AND ("balloon-occluded TACE" OR "B-TACE" OR "balloon occlusion" OR "balloon-assisted chemoembolization")).

Upon retrieval, records were screened for relevance, and duplicate or obviously unrelated publications were excluded. Bibliographic data, including publication year, authors, institutions, countries, and keywords, were exported from WoSCC for subsequent analysis. VOSviewer and Biblioshiny were used to visualize publication trends, institutional productivity, international collaborations, and keyword co-occurrence networks. The resulting bibliometric maps provided a comprehensive overview of the evolution of B-TACE research and helped identify major research hotspots in the field.

The bibliometric results are presented in Figure 1. Annual scientific production remained relatively limited in the early years but showed an overall increasing trend after 2013, with noticeable publication peaks in recent years, reflecting increasing attention to B-TACE in HCC.

At the institutional level, Sapienza University of Rome ranked first in publication output, followed by the University of Ulsan and Sun Yat-sen University, indicating that the field has been driven by several active research centers.[12] The country collaboration network showed that Japan was a major contributor to this topic, whereas Italy occupied a central position in international collaboration. In the keyword co-occurrence map, HCC, TACE, balloon occlusion, embolization, and chemoembolization were the most prominent terms, suggesting that current research mainly focuses on technical optimization, hemodynamic mechanisms, local tumor control, and multimodal treatment strategies. These findings validate the growing clinical and academic relevance of B-TACE and provide vital context for the following discussion of its mechanisms, indications, efficacy, and safety.

## B-TACE procedure

### *Mechanism*

The optimal management of TACE-refractory HCC remains unclear, with impaired survival often reflecting both tumor progression and repeated TACE-induced liver dysfunction. Thus, the selection of tailored therapy is crucial. Previous studies indicate that B-TACE achieves enhanced lipiodol accumulation and promising local tumor control.[9,13–15]

Consequently, B-TACE has garnered substantial attention and emerged as a promising therapeutic modality for HCC in recent years. Selective occlusion of the hepatic artery using a microballoon catheter allows the injection of lipiodol emulsion under reduced arterial pressure. This leads to early stagnation of arterial flow in the normal liver parenchyma owing to the viscosity of the emulsion and a diminished arterioportal pressure gradient. In contrast, tumor vessels maintain relatively preserved flow owing to their low vascular resistance, thereby restricting lipiodol entry into normal tissues while promoting its selective accumulation within the tumor.

Additionally, by preventing the backflow of agents and enabling pressurized infusion, the balloon minimizes non-target leakage and promotes deeper penetration of lipiodol and em-

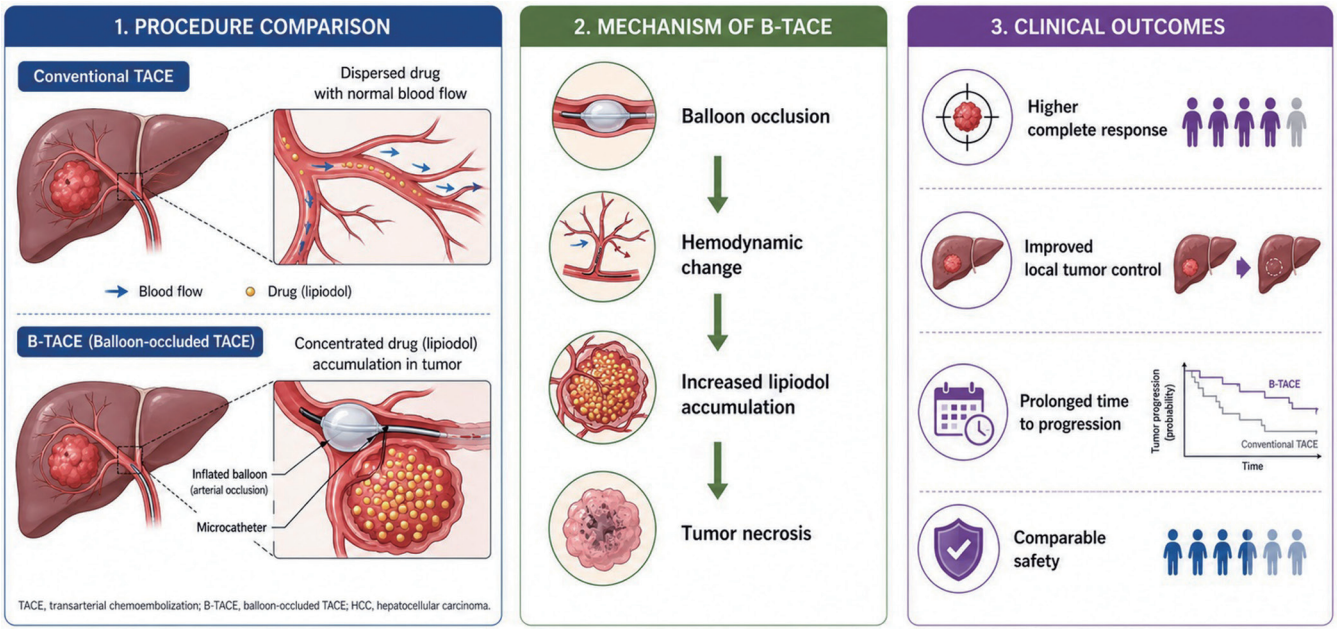


**Fig. 2. Mechanism of B-TACE.** B-TACE, balloon-occluded transarterial chemoembolization.

bolic material into the tumor, thereby enhancing therapeutic efficacy (Fig. 2). This superior embolization profile, achieved regardless of the embolic agent, was confirmed *in vivo*.[11]

Therefore, balloon occlusion is projected to offer two advantages: promotion of drug accumulation via hemodynamic modification and streamlined delivery by reducing the number of target vessels through a sustained pressure gradient. Nevertheless, therapeutic efficacy is significantly dependent on both balloon placement and injection pressure, making precise catheter deployment in the subsegmental or segmental arteries essential. While indications continue to be refined based on tumor characteristics, B-TACE is particularly suited for patients with challenging anatomy or an inadequate response to C-TACE.[16–18]

### *Hemodynamic changes during B-TACE of HCC*

Asayama *et al.*[19] demonstrated that poor treatment efficacy was linked to various balloon-occluded computed tomographic hepatic angiography (BO-CTHA) patterns, including the presence or absence of coronal staining and the appearance of reduced perfusion defects, compared with standard computed tomographic hepatic angiography (CTHA). Their analysis further revealed that the pattern of reduced perfusion defects on BO-CTHA was associated with a significantly poorer treatment effect than other patterns, such as those with or without coronal staining or with normal perfusion. Furthermore, Yoshimatsu *et al.*[20] found that a suboptimal therapeutic outcome was associated with tumors located in the central region, as well as with insufficient tumor staining observed on BO-CTHA.

Sugimoto *et al.*[21] suggested that the utilization of contrast-enhanced ultrasound was instrumental in facilitating B-TACE, as it allows intraprocedural flow monitoring, which contributes to superior procedural performance and more dependable outcomes. Ishikawa *et al.*[22] reported that intertumoral arterial flow can undergo changes following balloon occlusion, presumably because of the establishment of collateral pathways. Consequently, HCC lesions exhibiting decreased pixel values on subsequent cone-beam computed tomography (CBCT) are associated with poorer short-term therapeutic effects of B-TACE than those showing an increase.

### *Balloon-occlusion microcatheter type*

The introduction of microballoon catheters in Japan spurred the development of B-TACE.[9] As reported in previous studies, the balloon-occlusion microcatheters currently used in B-TACE include Sniper (Emboix, USA),[23] Attendant Delta, Occlusafe (Terumo, Japan),[9,14,24] Logos (Piolax, Japan),[13] and Distail Bonbon (APT Medical, Hunan, China).[25]

Compared with conventional microcatheters, balloon-occlusion microcatheters feature a balloon that can be repeatedly inflated and positioned at a specific distance from the catheter tip. Upon inflation, the balloon is anchored proximally within the target vessel, effectively interrupting antegrade blood flow to prevent reflux of embolic materials, thereby achieving precise embolization. Moreover, to ensure denser packing of embolic agents within the target vasculature, this catheter enables relatively high-pressure injection during the delivery process. This technique is known as pressure-directed embolization.

### *B-TACE process*

Irie *et al.* first demonstrated *in vivo* that flow redistribution occurred at a balloon-occluded arterial stump pressure (BOASP) of ≤ 64 mmHg.[9] At this pressure, both drugs and embolics penetrate tumor and feeder vessels more deeply, and the lipiodol emulsion concentration ratio (HCC versus embolized parenchyma) is significantly higher than that achieved at BOASP > 64 mmHg (Figs. 3 and 4). Following this initial observation, balloon occlusion has been consistently associated with elevated intratumoral drug levels. Rose *et al.* later quantified this benefit, showing that B-TACE delivered a significantly greater mean dose of drug/emulsion than C-TACE.[26]

B-TACE consists of four sequential steps. Following careful insertion of the balloon catheter into the tumor-feeding artery, the balloon is inflated to achieve vascular occlusion. Subsequently, chemotherapy and embolic agents are infused

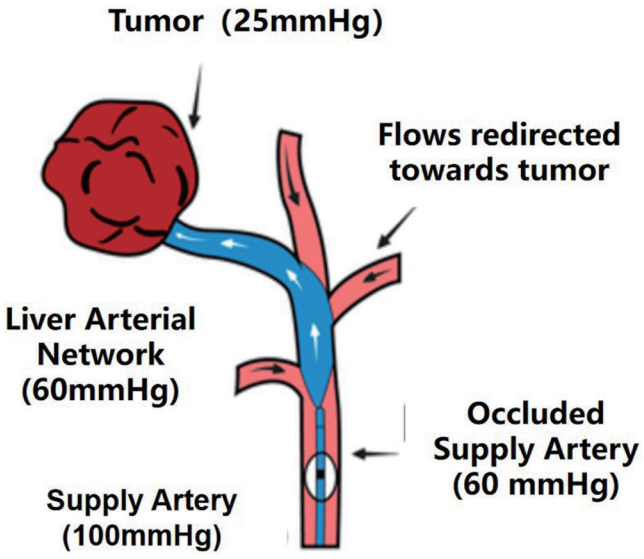


**Fig. 3. Low-pressure state with multiple arterial feeders.** The balloon is inflated to occlude the feeding artery, thereby reducing distal blood pressure. Under low-pressure injection conditions, the embolic agent or chemotherapeutic drugs preferentially flow into vessel branches with the lowest pressure. Before embolization, low-pressure contrast injection is performed to confirm that the agent is distributed solely to the tumor region.

directly into the isolated vascular bed. Finally, the balloon is deflated, and the catheter is removed. This sequence ensures targeted deposition of embolic material, which effectively blocks the tumor microvasculature, cuts off oxygen and nutrient supply, and leads to progressive cancer cell death.

To optimize B-TACE pressure-gradient effects, standard TACE techniques and materials must be modified. Preprocedural imaging identifies all feeders and guides microballoon placement proximal to them. After coaxial catheterization, vessel caliber is assessed by digital subtraction angiography (DSA) to select the balloon diameter. Inflation in straight segments is preferred, whereas curved vessels require stabilization. Continuous pressure monitoring via the wire lumen detects tip pressure changes—the only reliable method to avoid overinflation, which may cause spasm, dissection, or pseudoaneurysm. Inflation stops at pressure drop (target approximately 64 mmHg); no pressure drop suggests competitive feeders. Postinflation DSA confirms flow redistribution; an unchanged appearance again suggests competitive

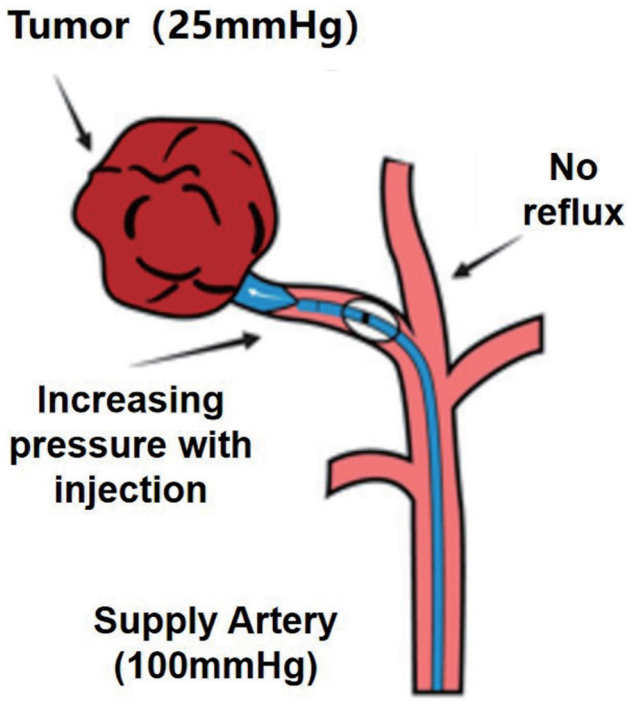


**Fig. 4. High-pressure state with exclusive tumor arterial supply.** The balloon is inflated to occlude the feeding artery, creating an isolated target territory. Under high-pressure injection, reflux is avoided, and the drug concentration is significantly increased.

supply. Embolization uses beads or lipiodol. Endpoints differ from standard TACE (10-heartbeat stasis): (1) resistance to injection, (2) reflux despite balloon occlusion, and (3) collateral flow reversal. If hepatofugal collaterals appear, the procedure should be stopped to avoid embolic migration to healthy parenchyma. Continuous fluoroscopy is mandatory.

The clinical indications and key technical considerations for optimizing B-TACE according to current evidence are summarized in Table 1.

## Therapeutic effect of B-TACE

### *B-TACE compared with C-TACE*

Both single-center[27] and multicenter studies have consist-

**Table 1. Indications and technical considerations for B-TACE**

| Category | Factors | Description / Recommendation |
|---|---|---|
| Indications | Tumor size | Optimal for 3–5 cm lesions |
| | C-TACE-refractory disease | Effective salvage therapy |
| | Vascular anatomy | Suitable for complex or multiple feeders |
| | Bridge therapy | Prior to resection or transplantation |
| Technical factors | Balloon position | Subsegmental or more peripheral placement recommended |
| | BOASP | < 64 mmHg associated with better drug delivery |
| | Injection technique | Pressure-directed embolization |
| | Imaging guidance | CBCT or CEUS improves targeting |
| | Embolic agents | Lipiodol-based or drug-eluting agents |

BOASP, balloon-occluded arterial stump pressure; CBCT, cone-beam computed tomography; CEUS, contrast-enhanced ultrasound.

**Table 2. Summary of key clinical studies evaluating B-TACE in hepatocellular carcinoma**

| Author (Year) | Study design | Sample size | Comparison | Tumor characteristics | Key outcomes | Main findings |
|---|---|---|---|---|---|---|
| Chu *et al*.[27] (2023) | Retrospective (PSM) | 567 (32 pairs) | B-TACE vs. C-TACE | Solitary HCC (>3 cm) | CR: 93.8% vs. 62.5% | Higher CR and prolonged LTP with B-TACE |
| Golfieri *et al*.[31] (2021) | Multicenter (PSM) | NR | B-TACE vs. C-TACE | Stratified by size | Higher CR in 30–50 mm tumors | B-TACE superior in intermediate tumors |
| Lucatelli *et al*.[28] (2021) | Case-control | 149 patients | B-TACE vs. DEB-TACE | Mixed sizes | ORR (9–12 mo): 78.9% vs. 53.9% | Better long-term tumor control with B-TACE |
| Kim *et al*.[30] (2020) | Retrospective | NR | B-TACE after C-TACE failure | Refractory HCC | ORR: 100% | Effective in C-TACE-refractory cases |
| Lucatelli *et al*.[29] (2022) | Interventional | 23 patients | B-TACE + MWA | Localized HCC | CR (1 mo): 91.3% | High efficacy in combination therapy |

PSM, propensity score matching; B-TACE, balloon-occluded transarterial chemoembolization; C-TACE, conventional transarterial chemoembolization; DEB-TACE, drug-eluting bead transarterial chemoembolization; MWA, microwave ablation; HCC, hepatocellular carcinoma; CR, complete response; ORR, objective response rate; LTP, local tumor progression; NR, not reported.

ently demonstrated that, after applying propensity score matching (PSM) to control for potential confounders,[17] B-TACE shows superior outcomes compared with C-TACE in terms of complete response (CR) rates, time to local tumor progression (LTP), and retreatment rates. Furthermore, accumulating evidence from multiple investigations strongly supports the preferential use of B-TACE as a treatment strategy for HCC, particularly in cases of intermediate-sized tumors (30–50 mm) identified through preprocedural imaging. Moreover, the reproducibility of these favorable results across different study settings not only validates the efficacy of B-TACE but also suggests its potential to provide improved therapeutic outcomes in HCC management.

Key clinical studies evaluating the efficacy of B-TACE in HCC are summarized in Table 2.[27–31] Overall, B-TACE demonstrates superior CR rates and improved local tumor control compared with C-TACE techniques, particularly in intermediate-sized tumors.

Chu *et al*.[27] conducted a single-center retrospective study to compare the efficacy and safety of B-TACE and C-TACE for solitary HCC treatment. Of the 567 enrolled patients (44 undergoing B-TACE and 523 undergoing C-TACE), PSM generated 32 well-balanced pairs for comparative analysis. The results demonstrated that B-TACE achieved significantly superior outcomes, with a markedly higher initial CR rate (93.8% vs. 62.5%) than C-TACE. During the median 37-month follow-up period, LTP occurred in 40.6% of B-TACE cases and 50% of C-TACE cases. Notably, B-TACE significantly prolonged the median time to LTP in medium-to-large HCCs (>3 cm). The major complication rates were comparable between the groups.

Golfieri *et al*.[17] reported that both C-TACE and B-TACE demonstrated high overall response rates, with C-TACE showing marginally better results, likely because of its superior efficacy in smaller lesions (<30 mm). However, in intermediate-sized HCCs (30–50 mm), B-TACE achieved a significantly higher CR rate, whereas in larger lesions (>50 mm), both techniques performed similarly, yielding poor CR rates. Lucatelli *et al*.[28] compared B-TACE with DEB-TACE in patients with HCC and found that, although the two methods had comparable safety profiles, B-TACE was associated with a more favorable oncological response and prolonged time to recurrence (TTR), notably in cases involving larger tumors.

### *B-TACE compared with DEB-TACE*

B-TACE shows a tendency toward superior long-term tumor control and delayed recurrence compared with DEB-TACE, particularly in HCC patients with larger tumors, while maintaining a comparable safety profile.[28]

In a single-center, case-control study by Lucatelli *et al*.,[28] the oncological outcomes and safety profiles of B-TACE and DEB-TACE were compared in patients with HCC. The study included 149 patients (226 tumors), of whom 22 underwent B-TACE and 127 underwent DEB-TACE. While tumor response assessed by the mRECIST criteria was comparable between the two groups at 1 and 3–6 months, B-TACE demonstrated a significantly higher overall response rate at follow-up (9–12 months: 78.9% vs. 53.9%). Moreover, B-TACE was associated with a favorable trend in TTR after CR (278.0 days vs. 219.0 days). Notably, the safety profiles of the two techniques remained similar, with no significant differences in adverse event (AE) rates.

### *B-TACE combined with SIRT or ablation therapy*

Lucatelli *et al.*[11] conducted a comparative analysis of 2D/3D dosimetry between SIRT and balloon-occluded SIRT (B-SIRT) using single-photon emission computed tomography (SPECT)/computed tomography (CT) imaging. In their study, SPECT/CT scans were performed 1–20 h after SIRT to evaluate the distribution of $^{90}$Y microspheres, with particular focus on assessing the accuracy and intensity of $^{90}$Y resin microsphere activity distribution. Both 2D and 3D analyses demonstrated that B-SIRT had superior dosimetric characteristics. Specifically, in the 2D evaluation, the B-SIRT subgroup showed a significantly higher peak activity intensity than conventional SIRT [(987.5 ± 393.8) vs. (567.7 ± 302.2), $P$ = 0.005], indicating that more $^{90}$Y microspheres were delivered to the target area at equivalent administered activity. Regarding 3D dosimetric analysis, the B-SIRT group achieved a significantly higher mean dose delivery to the treatment site [(151.6 ± 53.2) Gy vs. (100.1 ± 43.4) Gy, $P$ = 0.01], whereas the mean dose to normal liver tissue showed a minimal increase [(29.4 ± 5.7) Gy vs. (28.0 ± 8.8) Gy, $P$ = 0.70].

There are few reports on microwave ablation (MWA) combined with B-TACE. Lucatelli *et al.*[29] reported a study of 23 patients with HCC who underwent MWA with balloon microcatheter occlusion of the feeding artery, followed by B-TACE. The results demonstrated that the tumor necrosis volume was 103.2% of the ablation necrosis volume. Notably, no major intraoperative complications occurred, whereas post-embolization syndrome (PES) was observed in 12/23 cases

(52.2%). Regarding treatment efficacy, the 1-month follow-up revealed a CR rate of 91.3% (21/23) and a partial response (PR) rate of 8.7% (2/23). At 3–6 months after treatment, CR was maintained in 85.7% (18/21) of patients, with PR in 9.5% (2/21) and progressive disease (PD) in 4.7% (1/21).

### *Repeated alternate infusion B-TACE (RAIB-TACE)*

TACE is a standard treatment option for small HCC nodules located in proximity to the gallbladder serosa (GS). Nevertheless, achieving adequate tumor control via superselective TACE with a microcatheter remains challenging in such cases, presumably because multiple minute tumor-feeding vessels may arise directly from the main arterial trunk rather than from distal branches. Consequently, the development of a RAIB-TACE technique specifically designed for GS-adjacent small HCC lesions represents a critical clinical priority.

Recently, a lipiodol-free TACE protocol using cisplatin and 1-mm porous gelatin particles was reported to be effective and safe for treating multiple hepatic nodules.[32] Irie *et al.* subsequently refined this method by employing a microballoon catheter and crushing the 1-mm particles into smaller fragments (130–200 μm in length) to enhance antitumor activity.[33] Under balloon occlusion, cisplatin infusion is expected to increase drug concentration within tumors, while the smaller gelatin fragments can penetrate lesions and simultaneously block collateral arterial supply. They initially applied this novel B-TACE variant, defined as RAIB-TACE, to GS-adjacent nodules that were refractory to conventional lipiodol TACE to assess its therapeutic efficacy. As a result, the objective response rate (CR or PR) to RAIB-TACE was 100% (CR, 93%; PR, 7%), whereas that in the Lip-TACE group was 62.1% (18/29). The findings demonstrate that RAIB-TACE yields significantly higher objective response rates than lipiodol TACE/B-TACE in patients with small HCC adjacent to the GS.

While numerous feeders render selective catheterization challenging in C-TACE, B-TACE reduces the number of required selections; however, it still poses technical difficulties, and therefore these nodules remain difficult to treat with either modality. Irie *et al.*[34] first reported the application of RAIB-TACE in large HCC nodules exceeding 7 cm. The objective response rate (CR + PR) was 100% (19/19), with 11 nodules showing CR and 8 showing PR; no nodule showed stable disease (SD) or PD.

When B-TACE was introduced in the 2000s, molecular-targeted agents were not available. TACE was the final treatment option for intermediate-stage HCC, and long-term CR was pursued even at the cost of liver parenchyma. Currently, owing to the availability of molecular-targeted therapies, preservation of liver function after TACE has become essential, and the therapeutic goal has shifted toward achieving short-term CR with minimal parenchymal damage. Because B-TACE reduces lipiodol deposition in nontumorous liver tissue, it may help preserve liver function compared with C-TACE. With the development of systemic therapies, the lipiodol dose used in B-TACE has been reduced, and RAIB-TACE is increasingly employed.

### *Indications for B-TACE*

For tumors ≥ 3 cm, radiofrequency ablation is generally not considered suitable because of the increased risk of incomplete ablation, irregular ablation geometry, and higher LTP rates. Hence, selective B-TACE offers a more reliable treatment option for such lesions. Conversely, for tumors ≥ 5 cm, a practical technical limitation exists in Japan, where the maximum allowable dose of lipiodol per session is 10 mL. Tumors exceeding 5 cm typically require more than 10 mL of lipiodol to achieve complete and homogeneous filling, making selective B-TACE with a single vial of lipiodol (10 mL) insufficient. Therefore, 5 cm represents a practical upper limit for optimal candidate selection.

B-TACE may offer a higher response rate and can serve as an alternative treatment for recurrent or refractory HCC after C-TACE. Kim *et al.*[30] reported B-TACE for HCC refractory to C-TACE, and the response rate to B-TACE according to the mRECIST criteria was 100% (CR, 75%; PR, 25%). Moreover, the median time to progression (TTP) following B-TACE was 5.3 months. B-TACE significantly prolonged the median TTP compared with the last C-TACE (4.4 vs. 2.7 months) in treating residual HCC. Barcelona Clinic Liver Cancer stage C and tumor multiplicity were identified as independent predictors of TTP after B-TACE. A retrospective multicenter study by Golfieri *et al.*[31] showed that the best target objective responses after PSM were similar for both B-TACE and non-B-TACE (90.1% vs. 86.8%) and that B-TACE achieved a significantly higher CR rate (59.3% vs. 41.8%) at 1–6 months, with a markedly lower retreatment rate (9.9% vs. 22.0%).

Therefore, B-TACE can serve as an effective bridging therapy for patients with HCC awaiting liver transplantation or resection. According to Kim *et al.*, a cohort of 25 consecutive patients with single HCC underwent subsegmental B-TACE as a bridge to planned hepatic surgery. On the initial follow-up CT, 72% of the patients exhibited oily subsegmentectomy; among these, 96% (24/25) achieved CR, whereas one patient showed PR. Subsequent pathological analysis revealed complete tumor necrosis in 72% (18/25) of cases, along with extensive peritumoral liver parenchyma necrosis. In contrast, the remaining seven patients demonstrated extensive HCC necrosis without significant peritumoral parenchymal involvement.[35]

Although determining the appropriate tumor size for B-TACE remains a central question, the findings of Golfieri *et al*. indicate that it serves as a first-line option for HCC lesions measuring 3–5 cm, whereas its benefit diminishes for larger lesions, often necessitating combination therapy.[17]

### *Suitable anticancer agents for B-TACE*

According to the previous literature, the most commonly used chemotherapeutic agent in B-TACE is miriplatin,[13–15,19,20,24,36] followed by cisplatin,[20,37] epirubicin,[38] and a mixture of doxorubicin hydrochloride and mitomycin.[9,39] Miriplatin is a lipophilic prodrug that undergoes *in vivo* biotransformation to dichloro(1,2-diaminocyclohexane)platinum, a species that forms covalent cross-links with DNA.[40] Its stable suspension in lipiodol facilitates selective retention within HCC and enables sustained drug release, characteristics that favor its application in B-TACE. Although comparative data against C-TACE agents (e.g., epirubicin, doxorubicin, and mitomycin C) remain scarce, reported response rates assessed according to treatment effect category 4 (TE4) criteria range from 20% to 40% at 13 months post-treatment.[41–44]

Recent studies have explored various chemotherapeutic combinations for B-TACE. Notably, some cases have demonstrated favorable outcomes with double platinum therapy combined with miriplatin and cisplatin.[45] Furthermore, Shirono *et al*. specifically compared anthracycline-based agents in B-TACE and reported significantly higher TE4 achievement rates with epirubicin-B-TACE than with miriplatin-B-TACE.[46] Similarly, Lucatelli *et al*. observed superior early treatment responses, with CR rates of 44.8% at 1 month and 52.9% at 3–6 months, accompanied by PR rates of 55% and 23.5%, respectively.[10] To date, no randomized controlled trials have

**Table 3. Complications associated with B-TACE and comparison with conventional TACE**

| Complication | Incidence | Mechanism | Severity | Comparison with C-TACE |
|---|---|---|---|---|
| Post-embolization syndrome | Common | Ischemia and inflammation | Mild–moderate | Similar |
| Elevated liver enzymes | Common | Hepatocyte injury | Mild–moderate | Similar |
| Hepatic artery pseudoaneurysm | Rare | Balloon-induced endothelial injury | Potentially severe | Higher (procedure-specific) |
| Liver abscess | Rare | Infection after embolization | Moderate–severe | Similar |
| Biloma | Rare | Bile duct ischemia | Moderate | Similar |

compared the efficacy of different anticancer drugs in B-TACE. Therefore, determining the optimal agent for this procedure requires further investigation.

### *Complications of B-TACE*

Furthermore, most previous studies have reported that complications associated with B-TACE, such as PES and elevated transaminase levels, are inherently linked to the TACE procedure itself. Specifically, when comparing the incidence of severe AEs (grade >3 according to the CTCAE criteria), including elevations in serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and white blood cell counts, no statistically significant differences were observed between B-TACE and conventional non-B-TACE techniques (such as C-TACE or DEB-TACE).[13,15] A systematic review by Sui *et al.* analyzed the efficacy and safety of B-TACE for HCC.[47] Patients receiving B-TACE experienced a significantly higher rate of PES compared with those treated with non-B-TACE. The incidence of grade 2 and grade 3 AEs did not differ significantly between patients treated with B-TACE and those receiving non-B-TACE. Substantial heterogeneity occurred in the PES outcome ($I^2$ = 76%) and moderate heterogeneity in grade 2 AEs ($I^2$ = 57%), whereas no heterogeneity was observed in grade 3 AEs ($I^2$ = 0%).

In contrast, the occurrence of hepatic arterial injuries, including pseudoaneurysms, is directly related to the use of microballoon catheters and is likely attributable to endothelial injury caused by balloon inflation.[48] This correlation suggests that technical factors, such as the ratio of the balloon inflation diameter to the target vessel diameter, warrant further investigation. Overinflation of the microballoon is the main cause of this complication. Prevention relies on careful observation of the catheter tip during balloon inflation. Air must be completely evacuated from the balloon channel, which should be confirmed by test inflation before catheter insertion. Pseudoaneurysms have been documented only in two case series, occurring as complications during the interventional radiologist's learning curve, with incidence rates of 1.1% and 2.8%, respectively.

Additionally, other complications, such as liver abscesses and bilomas following B-TACE, have been reported.[49,50] These complications are potentially influenced by the extent of embolization or the selection of embolic agent particle size. These aspects also require further elucidation in future studies.

The spectrum of complications associated with B-TACE is summarized in Table 3. Overall, the safety profile of B-TACE is comparable to that of C-TACE, although specific risks related to balloon catheter use should be considered.

### *Limitations of B-TACE*

Notwithstanding the encouraging outcomes reported to date, several clinical issues pertaining to B-TACE persist and warrant further investigation. First, B-TACE has been shown to improve the CR rate of target lesions, reduce the number of repeated TACE sessions, and lower the local recurrence rate in selected patients with HCC; however, its clinical application still faces several challenges. For instance, in patients with a larger tumor burden (>7 cm), it remains unclear whether B-TACE can yield superior clinical outcomes or whether it is associated with a higher incidence of severe complications; consequently, further evaluation is urgently needed in this specific subgroup. Second, the optimal treatment strategy for target lesions fed by multiple arterial feeders remains to be defined, specifically whether balloon-occluded microcatheters should be used to selectively catheterize each feeding artery individually or whether embolization should be directed solely to the dominant feeder. Third, it is uncertain whether B-TACE offers any advantage in hypovascular tumors, given that the balloon-occlusion technique relies on redistribution of arterial flow to hypervascular areas. Fourth, prolonged balloon inflation and overinflation inevitably injures the target vessel; therefore, more individualized protocols regarding balloon inflation pressure and duration, tailored to the diameter of the target vessel, should be established. Furthermore, although previous studies have compared B-TACE with other TACE modalities using PSM or inverse probability of treatment weighting, the sample sizes involved remain relatively small. To more comprehensively evaluate the efficacy and safety of B-TACE, larger-scale studies are warranted. Finally, multicenter studies and randomized controlled trials are needed to provide more robust evidence to support the clinical adoption of B-TACE.

### *Prospects of B-TACE*

Safety evaluations by Lucatelli *et al*. revealed no statistically significant differences in AE rates between B-TACE and DEB-TACE.[28] Interestingly, their findings highlighted the enhanced antitumor efficacy of DEB-TACE in cases of large HCCs, suggesting potential modality-specific therapeutic niches.

Comparative analyses of TACE techniques have demonstrated distinct therapeutic advantages of B-TACE for HCC management. Notably, B-TACE yields significantly prolonged local recurrence-free periods in completely necrotic (TE4) nodules compared with C-TACE and DEB-TACE, establishing its potential as a radical treatment option.[7] Furthermore, B-TACE demonstrates superior oncological outcomes relative to DEM-TACE, particularly in patients with larger tumors, as indicated by longer TTR while maintaining comparable safety profiles.[28]

B-TACE demonstrates promising efficacy and safety profiles compared with C-TACE and DEB-TACE in previous studies. Current evidence suggests that it may be associated with improved CR rates and prolonged local recurrence-free

survival. Therefore, B-TACE may be considered a potential treatment option; however, further prospective, large-scale validation is needed.

The integration of CBCT and fusion imaging has significantly improved procedural planning and navigation for B-TACE. These technologies enable precise mapping of tumor vasculature and real-time catheter guidance, potentially improving technical success rates while reducing non-target embolization.

Artificial intelligence, particularly machine learning algorithms, shows promise for optimizing TACE outcomes. Recent systematic reviews have indicated that machine learning models can effectively predict objective responses to TACE and long-term survival, potentially aiding patient selection for B-TACE over alternative approaches.

The development of biodegradable embolic materials represents another advancement in B-TACE. These materials provide temporary vascular occlusion while eliminating permanent vascular damage, potentially preserving future treatment options.

## Conclusions

B-TACE has been established as a valuable technical refinement for the interventional management of HCC. Through its unique mechanism of balloon-occluded flow arrest, this technique achieves superior drug delivery and tumor penetration compared with C-TACE and DEB-TACE, particularly in cases with challenging vascular anatomy or TACE-refractory disease. The evolving landscape of HCC treatment increasingly emphasizes multimodal strategies, with B-TACE serving as an effective component of combination regimens that incorporate immune checkpoint inhibitors and targeted therapies. Ongoing technical innovations in imaging navigation, embolic materials, and patient selection algorithms are likely to expand the application and efficacy of B-TACE. Although further prospective validation would help refine patient selection criteria and standardize technical protocols, current evidence supports the growing integration of B-TACE into comprehensive HCC treatment programs, offering improved outcomes for patients with advanced disease.

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## Conflict of interest

The authors have no conflict of interests related to this publication.

## Author contributions

Conception and revision (NW, BL); literature search (BL, JL, QL, FT); Manuscript writing (BL, JL). All authors have approved the final version and publication of the manuscript.

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