

# Liver-Directed Therapy for Hepatic Malignancies

Murthy R. Chamarthy, MD, and Sanjeeva P. Kalva, MD

## Abstract

Locoregional therapies are well established in the treatment of primary and secondary hepatic malignancies and are aimed at a cure, bridging for definitive therapy or palliation. Such therapies include ablation (thermal, chemical, electroporation), hepatic artery-directed therapies (microsphere embolization, chemoembolization, selective internal radiation therapy with yttrium-90 particles), and radiation/proton therapy. This short review focuses on ablation and hepatic artery-directed therapies, and aims to provide a brief overview, indications for therapy, and outcomes from selected trials.

**Key words:** hepatocellular cancer, liver malignancy, ablation, transarterial chemoembolization, radioembolization, microwave ablation, radiofrequency ablation, metastasis

## Introduction

Liver-directed therapies for hepatic malignancies are used either in isolation [usually for hepatocellular carcinoma (HCC)] or in combination with systemic chemotherapy and/or surgery (for metastases or cholangiocarcinoma). Their role in the management of hepatic malignancies has progressed from being palliative in nature (hepatic artery-directed therapies) to curative with the introduction of ablative therapies and combination therapies (ablation plus hepatic artery-directed therapies). Additionally, these therapies form an integral part of hepatic transplantation for HCC by downsizing or controlling the tumor growth while patients await hepatic transplantation. In case of metastatic tumors, ablative therapy is often used as an adjunct to surgical resection, either to limit the extent of surgery or to treat bilobar disease. Despite the varied nature of these therapies, they all aim at providing minimally invasive therapy (as compared with surgery), minimizing the systemic effects of oncological therapy (as opposed to systemic chemotherapy), and minimizing the harmful effects on normal liver tissue while providing adequate tumor control. In addition, some of these therapies (eg, yttrium-90 [Y-90] radioembolization) appear to

have a synergistic effect with systemic chemotherapy in achieving tumor control. We will discuss these therapeutic options in the management of HCC and hepatic metastases.

## Hepatocellular Carcinoma

The detection and subsequent outcomes of HCC in an at-risk population are highly dependent on the surveillance programs. Small and unifocal tumors benefit from curative therapies, whereas larger and multifocal tumors typically are managed by palliative therapies. In addition, unlike other malignancies, therapy for HCC is highly dependent on the stage of underlying chronic liver disease.<sup>1</sup> Barcelona Clinic Liver Classification (BCLC) stratifies the HCC population into very early, early, intermediate, advanced, and terminal groups, with management recommendations based on the size and number of lesions, presence of venous invasion or extrahepatic metastases, Child-Pugh status, and Eastern Cooperative Oncology Group (ECOG) functional status.<sup>2</sup>

Curative therapies include hepatic transplantation, surgical resection, and ablation. Hepatic transplantation provides the best outcomes because it replaces the tumor and the cirrhotic liver that predisposes to subsequent tumors. Given the small number of available donor livers, defined criteria (eg, Milan, University of California, San Francisco) are used to select patients for optimal outcomes following hepatic transplantation.<sup>3,4</sup> Surgical resection is reserved for the minority of patients presenting with early disease (3 nodules <3 cm each or 1 lesion <5 cm), no vascular invasion or extrahepatic spread, absence of portal hypertension, and good liver function (Child Pugh A status) and performance status (PS; ECOG PS 0). Ablation is considered a curative therapy for very early (single lesions <2 cm, Child-Pugh A status, and ECOG PS 0) and early-stage HCC, and is practiced in patients who are not eligible for surgical resection. Multifocal and bilobar tumors in asymptomatic patients with Child Pugh A/B status and good PS are managed with transarterial therapies. Advanced disease in patients presenting with symptoms, portal or hepatic venous invasion, and extrahepatic spread are triaged to either systemic therapy with sorafenib (Child Pugh A/B status and ECOG PS 1-2) or symptomatic therapy (Child Pugh C status

**TABLE 1.** Role of Ablation in the Treatment of HCC

Population, Type of Study	Setting/Premise	Results	Reference
N = 161, resectable HCC; RCT	RFA vs surgery	Similar 4-year OS (67.9 vs 64) and DFS (46.4% vs 51.6%)	Chen et al, 2006 <sup>64</sup>
N = 105, resectable HCC; RCT	RFA vs surgery	Similar 3-year OS (87.1 vs 86.4) and DFS (51.3% vs 82.34%)	Lu et al, 2006 <sup>65</sup>
N = 232. HCC; RCT	RFA vs PEI	Improved 4-year OS (74% vs 57%); smaller risk of death, recurrence, and local progression (46%, 43%, and 88%, respectively)	Shiina et al, 2005 <sup>66</sup>
N=117, HCC; retrospective	RFA + TACE vs surgery	Similar OS at 1, 3, and 5 years	Kagawa et al, 2010 <sup>67</sup>
N = 360, HCC; RCT	Cryoablation vs RFA	Improved local tumor progression rates at 1, 2, and 3 years (3%, 7%, and 7%, respectively vs 9%, 11%, and 11%, respectively); no difference in tumor progression and OS rates	Wang et al, 2015 <sup>68</sup>
N = 107, HCC; retrospective	MWA vs surgery	Similar 1-, 3-, and 5-year OS; lower DFS with MWA if Milan criteria met or similar DFS for solitary <3 cm HCC	Shi et al, 2014 <sup>69</sup>
N = 53, HCC; retrospective	RFA vs MWA	Similar response, recurrence, and PFS rates	Vogl et al, 2015 <sup>11</sup>

DFS, disease-free survival; HCC, hepatocellular carcinoma; MWA, microwave ablation; OS, overall survival; PEI, percutaneous ethanol injection; RCT, randomized controlled trial; RFA, radiofrequency ablation; TACE, transarterial chemoembolization.

and ECOG PS 3-4). However, a select group of such patients may potentially benefit from transarterial therapies, especially those with limited venous invasion and relatively preserved liver function and PS.<sup>2,5</sup>

The reported 5-year survival in the very early and early-stage HCC among those treated as per the BCLC algorithm is 50% to 70% compared with 20% in the untreated population.<sup>6</sup> Chemoembolization improves survival in the intermediate stage of HCC, with reported median survival of 20 months compared with 16 months in the untreated population. In the advanced stage, sorafenib therapy is associated with improved median survival (10.7 months vs 7.9 months).<sup>7</sup> Transarterial therapy in a select group of patients with advanced stage improved median survival (13.3 months).<sup>5</sup> Outcomes in the terminal stage HCC are poor (<3 months).<sup>6</sup>

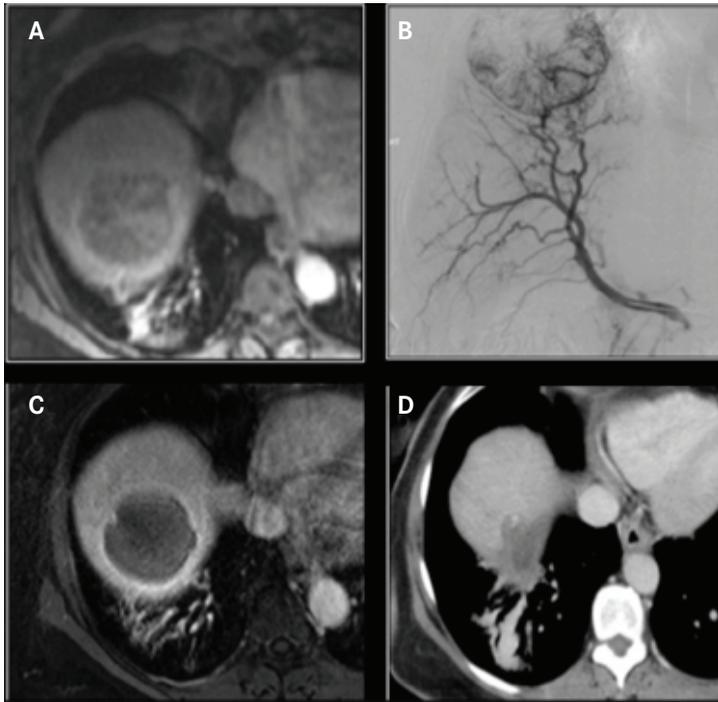
### Ablative Therapies

Ablative therapies destroy the tumors by selective deposition of thermal energy (radiofrequency ablation [RFA], microwave ablation [MWA], cryoablation) or disruption of the cellular membranes (irreversible electroporation), or cellular dehydration and disruption of endothelial cell integrity (chemical ablation), resulting in cellular death. Chemical ablation, performed through intratumoral injection of ethanol or acetic acid, is associated with higher rates of recurrence and complications, and has largely been replaced with other ablative modalities. The current role of chemical ablation is limited for treatment of very small lesions (<2 cm), small residual disease following

other ablative therapies, and as an adjunct to ablation in the treatment of a tumor that is adjacent to vital structures/blood vessels.<sup>8,9</sup>

In RFA, a high frequency alternating current (450–500 kHz) is passed through an electrode (the probe that is placed into the tumor). This results in frictional heat (50 degrees C–105 degrees C) generation, and the heat is conducted into the surrounding tumor cells, leading to coagulative necrosis and cell death. Radiofrequency ablation is widely available, extensively studied, and is an established treatment modality. The main limitations of RFA relate to decreased or nonuniform heat distribution resulting in higher local recurrence rates in the presence of adjacent high-flow blood vessels (“heat sink effect”) and from charring/dessication around the probe.<sup>10</sup> Microwave ablation uses electromagnetic waves that result in the vibration of water molecules within the tissue, leading to heat generation and cellular death. Microwave ablation is less time-consuming compared with RFA, and allows for excellent uniform heat distribution without any heat sink from adjacent vessels. Despite the theoretical benefits of MWA, studies report similar outcomes compared with RFA.<sup>11</sup> Freezing from rapid expansion of gas through a low-pressure probe in combination with thawing cycles during cryoablation results in intracellular dehydration and cell death. Cryoablation is well suited for ablation of tumors that are in proximity to vital structures, and offers the ability for real-time monitoring of the treatment zone. However, cryoablation carries the risks of hemorrhage (<2%) and cryoshock (2%), especially in patients with underlying cirrhosis

**FIGURE.** 58-Year-Old Female with Hepatitis C Cirrhosis, Intermediate HCC



A 58-year-old female with hepatitis C cirrhosis, intermediate-stage hepatocellular carcinoma (HCC) presents with a 4.5-cm segment VIII HCC on MRI scan (A). Right hepatic arteriogram demonstrates hypervascular HCC (B) corresponding to the MRI findings, and DEB-TACE was performed. MRI scan at 1 month (C) and CT scan at 18 months (D) postchemoembolization demonstrated complete response without any residual disease or recurrence.

larger tumors can be successfully treated with a combination of RFA and chemoembolization.<sup>23,25</sup> The sequence of these procedures is not standardized, but the authors of this article typically practice chemoembolization first, followed by ablation. This approach has two advantages: (1) the tumor can be successfully “stained” with lipiodol during transarterial chemoembolization (TACE) that allows visualization of the tumor on noncontrast computed tomography (CT) for easy targeting during ablation; and (2) embolization decreases the risk of heat sink effect. Laparoscopic ablation is useful for lesions adjacent to the pericardium and the dome of the diaphragm, although the latter could be approached percutaneously through a transpleural route by creating an artificial pneumothorax.<sup>26</sup> Ablative therapies are safe, but risks include pain (for lesions adjacent to the diaphragm or abdominal wall), bleeding, and injury to adjacent vital structures such as the biliary system.<sup>27</sup> The results of ablation for HCC are summarized in **Table 1**.

#### Transarterial Therapies

Transarterial therapies take advantage of differential blood supply of the tumors (supplied by the hepatic artery) and normal liver parenchyma (predominantly supplied by the portal vein), and high microvessel density within the tumors resulting from tumoral angiogenesis. The commonly applied transarterial therapies involve various microembolic materials, and include particle embolization without any chemotherapy (also called transarterial embolization [TAE] or bland embolization), chemoembolization with lipiodol-chemotherapy emulsion and microparticles or gel foam (conventional chemoembolization [cTACE]), chemoembolization with drug-eluting microspheres (DEB-TACE), and Y-90 microsphere radioembolization. These therapies result in tumor ischemia, and the level of arteriolar/precapillary occlusion is dependent on the size of the beads. Given the ischemic effects, these therapies are associated with postembolic syndrome manifested by fever, pain, malaise, fatigue, and mild to moderate alterations in liver function tests. These symptoms most often are associated with TAE, cTACE, and DEB-TACE, and less commonly with Y-90.

#### Transarterial Embolization

Transarterial embolization is achieved with various microparticles of 40 microns to 700 microns in size. The smaller the particle size, the better the tumor necrosis, but the higher the risk of biliary injury. The tumor is targeted through highly selective catheterization of segmental or subsegmental arteries

and coagulopathy.<sup>12,13</sup> Other ablative therapies such as laser and high-intensity focused ultrasound are of limited proven utility in the treatment of HCC lesions, but may have an added benefit when combined with other therapies.<sup>14</sup> Ablation is recommended for very early and early-stage HCC as an alternative to surgical resection, and for downstaging/bridging considerations of intermediate-stage HCC prior to hepatic transplantation.<sup>15,16</sup> Despite conflicting data, ablation for very early and early-stage HCC is considered to be as effective as surgical resection with similar survival outcomes.<sup>17-20</sup> An ideal lesion for ablation is a small (<3 cm), peripheral, noncapsular HCC that is distant from the vital structures (gall bladder, common bile duct, diaphragm, and pericardium) and vasculature. Multiple lesions can be ablated, but procedure times and technical issues limit its use for up to three lesions during one treatment session. Tumors larger than 3 cm are routinely triaged to other regional therapies due to the risk of local recurrence with RFA. However, MWA, which allows synchronized tumor ablation with multiple probes and combination of RFA, and chemical ablation allow treatment of larger tumors (up to 5 cm) with great success.<sup>21,22</sup> Additionally,

**TABLE 2.** Role of Chemoembolization in the Treatment of HCC

Population, Type of Study	Setting/Premise	Results	Reference
N = 80, HCC; RCT	TACE vs conservative	Improved 1-, 2-, and 3-year survival rates (57%, 31%, 26%, respectively vs 32%, 11%, 3%, respectively)	Lo et al, 2002 <sup>70</sup>
N = 112, HCC; RCT	TACE vs bland embolization vs conservative	Improved 1- and 2-year survival probabilities (82% and 63%, respectively; 75% & 50%; 63% & 27%)	Llovet et al, 2002 <sup>29</sup>
N = 100, HCC; RCT	TACE vs systemic chemotherapy	Higher PR (32% vs 10%); median PFS (32 vs 26 weeks)	Mabed et al, 2009 <sup>71</sup>
N = 177, HCC; RCT (PRECISION ITALIA)	cTACE vs DEB-TACE	No difference in local and overall tumor response or survival rates	Golfieri et al, 2014 <sup>35</sup>
N = 307, HCC; RCT (SPACE trial)	DEB-TACE + sorafenib vs DEB-TACE	Prolonged TTP (HR, 0.797) and time to VI/EHS (HR, 0.621)	Lencioni et al, 2012 <sup>72</sup>
N = 192, HCC; prospective single-arm study (START trial)	TACE + sorafenib	CR: 52.6%; PR: 16.8%; disease progression: 5.8%; 3-year OS: 86.1%	Chao et al, 2015 <sup>40</sup>
N = 212, HCC; RCT (PRECISION V)	cTACE vs DEB-TACE	Higher rates of CR, ORR, and disease control without superiority (27% vs 22%, 52% vs 44%, and 63% vs 52%, respectively), but selective benefit in advanced cases, and decreased toxicity	Lammer et al, 2010 <sup>33</sup>

CR, complete response; cTACE, conventional transarterial chemoembolization; DEB-TACE, drug-eluting beads-transarterial chemoembolization; HCC, hepatocellular carcinoma; HR, hazard ratio; m: months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RCT, randomized controlled trial; RFA, radiofrequency ablation; TACE, transarterial chemoembolization; TTP, time to progression; VI/EHS, vascular invasion or extrahepatic spread.

supplying the tumor to minimize injury to normal hepatic parenchyma. The indications for therapy are similar to those of chemoembolization. The main advantage of this therapy over chemoembolization is the absence of chemotherapy-related side effects. Some studies suggest decreased effectiveness of TAE compared with DEB-TACE,<sup>28-30</sup> but others reported no significantly different outcomes.<sup>30</sup> A recent randomized study by Brown et al<sup>31</sup> reported equivalent efficacy of TAE compared with DEB-TACE in the treatment of HCC.

### Chemoembolization

Both cTACE and DEB-TACE allow targeted intra-arterial delivery of chemotherapeutic drugs to the tumor, with reduced systemic toxicity and side effects compared with systemic chemotherapy. Tumor death is achieved with chemotherapy in conjunction with the ischemic effect of the embolic materials. cTACE involves administration of lipiodol emulsified with doxorubicin, mitomycin C, and cisplatin. The clinical benefit of cTACE is well supported by randomized trials and is recommended for treatment of BCLC B tumors.<sup>29,32</sup> DEB-TACE (see **Figure**) offers the advantage of sustained and uniform intratumoral delivery of chemotherapy, and is superior to cTACE in terms of systemic toxicity and tolerability, especially in patients with decreased liver function.<sup>33,34</sup> The objective response rate (ORR) following

DEB-TACE is similar to that of cTACE, but superior in specific patient populations (eg, decreased liver function, bilobar disease, recurrent disease).<sup>33,35</sup>

The overall survival (OS) following chemoembolization is dependent on underlying liver disease, tumor burden, intravenous extension of the tumor, and extrahepatic metastases.<sup>36</sup> The number of chemoembolization procedures and tumor response following chemoembolization are associated with superior survival.<sup>5,36,37</sup> Recent reports suggest that DEB-TACE is safe and improves survival in patients with advanced HCC (BCLC C stage), especially in those with minimal symptoms, limited portal venous invasion, preserved liver function, and ECOG PS  $\leq 1$ .<sup>5,38</sup> Initial reports from a recent study investigating the role of concurrent sorafenib therapy during chemoembolization suggests no significant increase in toxicity, but survival benefits are unknown.<sup>39,40</sup> Results of chemoembolization are listed in **Table 2**. Most patients develop self-limiting postembolization syndrome (nausea, pain, fever) following chemoembolization. Complications of chemoembolization include liver failure (<5%); bone marrow suppression, renal failure, cardiac toxicity, abscess (<3%); and cholecystitis (<1%).<sup>41</sup> Bilio-enteric anastomosis, advanced liver disease, and prior chemotherapy increase the risk of postprocedure complications. In general, DEB-TACE has a superior safety profile compared with cTACE.<sup>34</sup>

**TABLE 3.** Role of Y-90 Radioembolization in the Treatment of HCC

Population, Type of Study	Setting/Premise	Results	Reference
N = 291, HCC; prospective cohort	Y-90 treatment response	WHO response rate: 42% EASL response rate: 57% TTP: 7.9 mo	Salem et al, 2010 <sup>73</sup>
N = 932, HCC; retrospective	Y-90 vs TACE vs conservative	Improved median OS (11.5 mo vs 8.5 mo vs 2 mo)	Carr et al, 2010 <sup>74</sup>
N = 245, HCC; retrospective	Y-90 vs. TACE	Higher response rate (49% vs 36%, longer TTP (13.3 mo vs 8.4 mo); no change in median survival times	Salem et al, 2011 <sup>42</sup>
N = 86, HCC; retrospective	Y-90 vs TACE for downstaging	Higher downstaging from T3 to T2 (58% vs 31%); higher PR, EFS, and OS rates; similar TTP	Lewandowski et al, 2009 <sup>75</sup>

CR, complete response; EASL, European Association for the Study of the Liver; EFS, event-free survival; HCC, hepatocellular carcinoma; mo, months; OS, overall survival; PR, partial response; RCT, randomized controlled trial; TACE, transarterial chemoembolization; TTP, time to progression; WHO, World Health Organization; Y-90, yttrium-90.

**Radioembolization**

When intra-arterially administered, particles that embed Y-90 are selectively deposited in the tumor microvasculature and release beta radiation from disintegration of Y-90 at an average half-life of 64 hours. The beta radiation has an average penetration of 2.5 mm and results in tumor cell death from brachytherapy. There are two commercially available Y-90 particles: resin microspheres (SIR-Spheres; Sirtex Medical Limited, North Sydney, Australia) and glass microspheres (TheraSpheres, MDS Nordion, Ottawa, Ontario, Canada). Apart from US Food and Drug Administration (FDA) approval status (SIR-Spheres for colorectal metastases in conjunction with systemic chemotherapy and TheraSpheres for HCC under humanitarian device exemption), there appears to be little difference in therapeutic effect and safety profile between the two Y-90 particles when used for hepatic malignancies. Although a high-dose ablative type segmental or lobar radioembolization (also known as radiation segmentectomy or lobectomy) has been well described,<sup>42,43</sup> radioembolization is routinely performed for multifocal tumors involving one or both lobes of the tumors at tumoricidal doses.

Given that the size of Y-90 particles (20 µm-60 µm ) is much smaller than those applied for chemoembolization and high toxicity associated with beta radiation, additional precautions are necessary during Y-90 therapy. A planning angiogram is performed to identify and occlude extrahepatic branches of the hepatic artery that might potentially lead to nontarget Y-90 distribution. Additionally, technitium-99m-labeled macro-aggregated albumin particles are intra-arterially administered to assess intra-hepatic particle distribution, and to calculate hepatopulmonary shunt that results from intratumoral arteriovenous communications. Subsequently, the Y-90 dose is calculated based on the tumor-to-liver ratio and lung shunt fraction, and is administered in the lobar or segmental arteries. High lung shunting (which can lead to radiation pneumonitis), extensive extrahepatic metastatic

disease, severe liver dysfunction, and difficult anatomy with uncorrectable nontarget distribution preclude Y-90 therapy.

A study by Salem et al<sup>42</sup> reported longer time to progression following Y-90 without significant change in OS when compared with cTACE and DEB-TACE. However, Y-90 was associated with less postembolic syndrome compared with cTACE/DEB-TACE, and was reported to be more cost-effective in a select group of patients.<sup>42,44,45</sup> In addition, Y-90 may be better tolerated in patients with intravenous tumor invasion. The comparative roles of Y-90 versus chemoembolization (PREMIERE trial<sup>46</sup>) and Y-90 versus sorafenib in advanced HCC (SARAH trial<sup>47</sup>) are being investigated. Postembolization syndrome following Y-90 occurs in 20% to 50% of patients. Complications of Y-90 therapy include Y-90 bowel injury (<5%), radiation pneumonitis (<1%), liver failure (0%-4%), biliary complications (<10%), radiation dermatitis, and bone marrow suppression.<sup>48,49</sup> The results of Y-90 treatment are listed in **Table 3**.

**Cholangiocarcinoma**

Cholangiocarcinoma has poor prognosis and typically presents at a locally advanced, unresectable stage. Recurrence rates are high following surgical resection. Extrahepatic metastatic disease at presentation is uncommon, allowing a greater role for locoregional therapies.<sup>50</sup> Radiofrequency ablation, TACE, and radioembolization are the treatment options with variable success based on the stage and extent of the tumor. A multi-institutional retrospective analysis demonstrated a median OS of 13.2 months, irrespective of the type of intra-arterial therapy.<sup>51</sup> A meta-analysis reported an OS of 22.8, 13.9, 12.4, and 12.3 months for hepatic arterial infusion, Y-90, cTACE, and DEB-TACE, respectively.<sup>52</sup>

**Hepatic Metastases**

Surgical resection is the mainstay for treatment of hepatic

**TABLE 4.** Role of Locoregional Therapy for Colorectal Metastatic Disease

Population, Type of Study	Setting/Premise	Results	Reference
N = 74, mCRC; RCT	DEBIRI vs systemic chemotherapy	Higher median OS (22 mo vs 15 mo); longer PFS (7 mo vs 4 mo)	Fiorentini et al, 2012 <sup>59</sup>
N = 979, mCRC; meta-analysis	Y-90 treatment response	Average CR: 0%; PR: 31%; median TTP: 9 mo; median OS: 12 mo	Saxena et al, 2014 <sup>56</sup>
N = 1373, mCRC; meta-analysis	Y-90 vs Y-90 + chemotherapy	Nonprogression (29%-90% vs 59%-100%); 1-year survival (37%-59% vs 43%-74%)	Rosenbaum et al, 2013 <sup>76</sup>

CR, complete response; DEBIRI, drug-eluting beads preloaded with irinotecan; mCRC, metastatic colorectal cancer; mo, months; OS, overall survival; PFS, progression-free survival; PR, partial response; RCT, randomized controlled trial; TTP, time to progression.

metastases from colorectal malignancy for the minority of patients who present at an early stage and qualify for surgery. For patients who are not surgical candidates, ablation, systemic chemotherapy, chemoembolization, and radioembolization are the treatment options. Ablation is recommended in the presence of a small number of lesions (<3), each measuring less than <3 cm, and for treatment of local recurrence along the surgical margins. In addition, ablation may be used as an adjunct to surgical resection in the presence of bilobar disease to avoid second-stage hepatectomy.<sup>53</sup> There are no randomized data comparing RFA with surgery; however, surgery offers superior local control of disease without a survival advantage. Transarterial therapies are typically considered with the failure of first-line and second-line chemotherapies and progression of disease, and include DEB-TACE using irinotecan (DEBIRI) and Y-90. When applied in the salvage setting, Y-90 has been shown to be effective in prolonging survival,<sup>54,55</sup> and the clinical benefit is dependent on tumor response on positron emission tomography (PET) scan and tumor burden. The reported median survival is 12 months, with improved survival in those who responded to therapy.<sup>54,56</sup> The application of Y-90 in combination with first-line and second-line chemotherapies has been shown to be beneficial in small studies.

The recent randomized studies comparing FOLFOX versus FOLFOX plus SIR-Spheres (SIRFLOX<sup>57</sup> and FOXFIRE<sup>58</sup>) demonstrated superior progression-free survival (PFS) with the latter, but no significant improvement in OS of patients with colorectal hepatic metastases. The role of DEBIRI is still evolving and appears to be effective in improving both PFS and OS.<sup>59</sup> The results of DEBIRI and radioembolization for hepatic metastases are listed in **Table 4**.

Hepatic metastases from neuroendocrine tumors are often indolent, but can be symptomatic from hormone secretion, capsular stretching, and tumor burden. Transarterial bland

embolization, chemoembolization, and radioembolization have been applied for locoregional control of the disease when surgery is not an option.<sup>60</sup> No randomized trials exist comparing various transarterial therapies. The outcomes of various transarterial therapies are similar with reported 1-, 2-, 3-, and 5-year survival of 85%, 63%, 46%, 50% with Y-90, respectively, and 75%, 66%, 48%, and 37% with TACE/TAE treatments, respectively.<sup>61</sup> Uveal melanoma has a high propensity for liver metastases despite successful treatment of the primary tumor. The prognosis is poor, and systemic therapy is relatively ineffective in the presence of hepatic metastatic disease. Locoregional therapy with hepatic arterial infusion, immunoembolization, chemoembolization, and radioembolization provide local control of hepatic disease and prolong survival. Median survival following Y-90 therapy ranges from 7 months to 10 months.<sup>62,63</sup>

### Conclusion

Management of hepatic malignancies requires a multidisciplinary approach, and is based on the tumor burden, liver function, and PS of the patient. Locoregional treatments offer a broad group of management options, with ablation in a potentially curative setting and intra-arterial therapies in a palliative or downstaging setting. Each of these locoregional treatments offers specific advantages and must be individualized to each patient for optimal outcomes.

**Affiliations:** Murthy R. Chamarthy, MD, and Sanjeeva P. Kalva, MD, are from the University of Texas Southwestern Medical Center, Dallas.

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**Address correspondence to:** Sanjeeva P. Kalva MD, Interventional Radiology, University of Texas Southwestern Medical Center, Dallas, TX 75390-8834; email: Sanjeeva.Kalva@UTSouthwestern.edu

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