Embolization of Parasitized Extrahepatic Arteries to Reestablish Intrahepatic Arterial Supply to Tumors before Yttrium-90 Radioembolization

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ABSTRACT

Purpose: To perform embolization of parasitized extrahepatic arteries (EHAs) before radioembolization to reestablish intrahepatic arterial supply to large, peripheral tumors, and to evaluate the technical and clinical outcomes of this intervention.

Materials and Methods: Among 201 patients retrospectively analyzed, embolization of 73 parasitized EHAs in 35 patients was performed. Most embolization procedures were performed during preparatory angiography using large particles and coils. Digital subtraction angiography (DSA), C-arm computed tomography (CT), and technetium-99m macroaggregated albumin (^{99m}TcMAA) scintigraphy were used to evaluate the immediate perfusion via intrahepatic collateral channels of target tumor areas previously supplied by parasitized EHAs. Follow-up imaging of differential regional tumor response was used to evaluate microsphere distribution and clinical outcome.

Results: After embolization, reestablishment of intrahepatic arterial supply was confirmed by both DSA and C-arm CT in 94% of territories and by scintigraphy in 96%. In 32% of patients, the differential response of treatment could not be evaluated because of uniform disease progression. However, symmetric regional tumor response in 94% of evaluable patients indicated successful delivery of microspheres to the territories previously supplied by parasitized EHAs.

Conclusions: Reestablishment of intrahepatic arterial inflow to hepatic tumors by embolization of parasitized EHAs is safe and effective and results in successful delivery of yttrium-90 microspheres to tumors previously perfused by parasitized EHAs.

ABBREVIATIONS

DSA = digital subtraction angiography, EHA = extrahepatic artery, PET = positron emission tomography, ^{99m}TcMAA = technetium-99m macroaggregated albumin

Radioembolization is an effective and safe treatment for patients with unresectable hepatic malignancy (1,2). Despite reports of, and trials on, radioembolization used as first-line therapy, it is frequently employed as a salvage therapy in patients who have undergone numerous other treatments, which may include surgical resection with or without portal vein embolization, transplantation, systemic chemotherapy and targeted agents, ablation, and intraarterial chemoembolization. Candidates for radioembolization tend to have advanced malignancy and may have intrahepatic arterial abnormalities and intraperitoneal adhesions—all conditions that predispose patients to forming parasitized extrahepatic arteries (EHA) that supply large or peripherally located hepatic tumors. Also found in 17% of patients receiving chemoembolization (3), parasitized EHAs disproportionately increase risk in patients receiving radioembolization because of the potentially severe consequences of nontarget radioembolization (4).

Preexisting intrahepatic collateral pathways can result in communication between one segment or lobe and another (5,6) and communication between extrahepatic arter-

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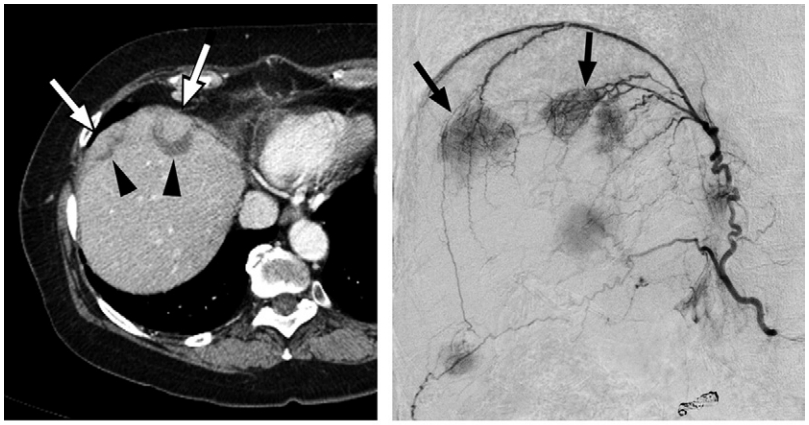
From the SIR 2010 Annual Meeting.

None of the authors have identified a conflict of interest.

J Vasc Interv Radiol 2011; 22:1355–1362

DOI: 10.1016/j.jvir.2011.06.007



a. b.

Figure 1. A 74-year-old woman with metastatic endometrial carcinoma underwent right lobe radioembolization at another institution and sought additional treatment. **(a)** Follow-up computed tomography (CT) scan 4 months after treatment showed necrosis of the inner aspects of the tumors (arrowheads) with residual or recurrent viable tumor on the juxtadiaphragmatic surface of the liver (arrows). **(b)** Angiography of the right inferior phrenic artery revealed parasitized extrahepatic arteries (EHAs) perfusing the hypervascular hepatic lesions (arrows). These parasitized EHAs were not recognized at the time of right lobe treatment, so the tumor territories they perfused were not adequately treated by radioembolization. Administration of radioembolic microspheres into the phrenic artery is contraindicated because of the risk of diaphragmatic injury and of intercommunication with the pulmonary circulation.

ies and the hepatic artery (7). We hypothesized that embolization of parasitized EHAs without devascularizing the tumors at the capillary level would result in the reestablishment of antegrade flow into these large or peripheral tumors from intrahepatic arteries, a strategy that has not previously been reported. This consolidation of hepatic arterial inflow would theoretically allow radioembolization treatment of tumors previously perfused by parasitized EHAs without incurring the high risk of nontarget radioembolization. We evaluated the technical success of reestablishing intrahepatic arterial supply to territories supplied by parasitized EHAs by analyzing postconsolidation imaging, including digital subtraction angiography (DSA), C-arm cone beam computed tomography (CT), and technetium-99m macroaggregated albumin (^{99m}TcMAA) scintigraphy. We also evaluated clinical success in distribution of microspheres by analyzing the differential objective responses of tumors previously supplied by parasitized EHAs compared with tumors directly supplied by normal intrahepatic arteries.

MATERIALS AND METHODS

All data were handled in compliance with the Health Insurance Portability and Accountability Act. The institutional review board of our institution approved this retrospective study.

Patients

Between June 2004 and December 2010, 201 patients underwent radioembolization by SIR-Spheres (Sirtex, Lane Cove, Australia; n = 161) or TheraSphere (MDS Nordion, Ottawa, Ontario, Canada; n = 40) for treatment of unresectable hepatic malignancy. Patient age ranged from 20–92 years (mean 60.1 y, median 61 y). We retrospectively reviewed all preparatory and treatment angiograms on these patients. Iterative data on individual patients who had undergone repeat radioembolization were also included. One patient was excluded from the analysis because she underwent a preparatory angiogram and right lobe treatment before our evaluation at another institution, where her parasitized EHA was not recognized (**Fig 1a** and **b**).

Complete Hepatic Angiography

Cross-sectional imaging with computed tomography (CT) or magnetic resonance (MR) imaging obtained before the procedure was reviewed in all patients before performance of angiography to identify high-risk tumors for parasitized EHAs. Attention was paid to tumors in contact with the diaphragm or in the bare area of the liver for the possibility of parasitized supply from the inferior phrenic artery; tumors near the right border of the liver for parasitized intercostal arteries; inferior tumors for parasitized renal, adrenal, lumbar, colic, and pancreaticoduodenal arteries; and superficial tumors and postsurgical recurrences surrounded by adipose tissue for parasitized omental arteries (8). Special attention was paid to possible parasitized internal mammary arteries supplying the anterior left lobe because of their undetectability on abdominal aortography.

The angiographic protocol included abdominal aortography with injection of contrast agent at the level of T8 to map the hepatic arterial anatomy and to visualize any hypertrophied extrahepatic vessels potentially providing parasitized supply to liver tumors. Both DSA and contrast-enhanced C-arm CT were performed with injection of contrast medium in the proper hepatic artery or common he-

patic artery, and hepatic territories devoid of parenchymal or tumor enhancement were identified as suspicious for being perfused by parasitized EHA.

All prominent or asymmetric arteries suspicious for parasitization identified on imaging or aortography before the embolization procedure were catheterized for selective arteriography. The cystic artery was considered to be within the intrahepatic treatment territory and was not catalogued as a parasitized EHA, even if it supplied arterial perfusion to tumors. The territories supplied by suspected parasitized EHAs were demarcated using selective contrast-enhanced C-arm CT.

Consolidation of Inflow by Embolization of Parasitized Extrahepatic Arteries

Embolization of identified parasitized EHAs was performed to stasis by using large particles (Embospheres 500–700 μm or 700–900 μm; Biosphere Medical, Inc, Rockland, Massachusetts) or a slurry of 1- to 2-mm cubes of gelatin sponge (Surgifoam; Ethicon/J&J, Somerville, New Jersey). The largest particles that could fit through the catheters used were chosen to occlude the parasitized EHA network of tumoral blood supply without reaching the capillary bed. Particles were used not to induce tumor ischemia but to minimize the potential for subsequent recruitment of other EHAs that could reestablish parasitized extrahepatic supply. After near-stasis was achieved, embolization of the main EHA was performed using 0.018-inch coils (eg, VortX; Target/Boston Scientific, Inc, Natick, Massachusetts; Tornado, MicroNester; Cook, Inc, Bloomington, Indiana; Azur; Terumo Medical, Somerset, New Jersey).

In situations where numerous side branches of a trunk were parasitized, coil embolization of the trunk distal to the origin of the parasitized branches was performed first, limiting the deposition of particles to the parasitized branches and reducing the risk of ischemia of the extrahepatic end organ. Finally, embolization of the proximal trunk was performed using coils to exclude the parasitized branches completely.

Imaging Confirmation of Consolidation and Intrahepatic Reperfusion

After embolization of parasitized EHAs, contrast-enhanced DSA and C-arm CT were repeated with injection of contrast agent in the main hepatic artery (proper hepatic artery or common hepatic artery) for confirmation of intrahepatic perfusion of the territory previously supplied by parasitized EHAs. In addition, from the planned site of administration of the microspheres, approximately 1 mCi of ^{99m}TcMAA was injected for scintigraphy. Patients underwent planar and single-photon emission computed tomography imaging to calculate the lung shunt fraction, to exclude extrahepatic perfusion, and to characterize the intrahepatic distribution of injected radiotracer.

At the time of the treatment procedure, we searched for interval recruitment of parasitized EHAs by repeat aortography. We also reevaluated success of consolidation and intrahepatic perfusion by repeating contrast-enhanced DSA and C-arm CT of the hepatic artery. If any additional or persistent parasitized EHAs were detected, these were managed in the same way as during preparatory angiography.

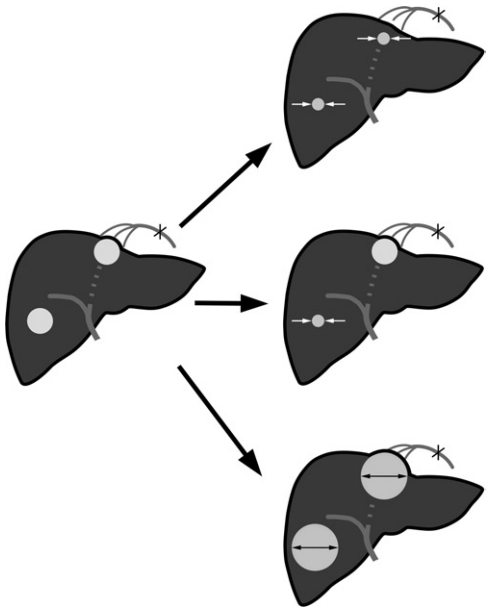


Figure 2. Assessment of microsphere distribution based on radiographic tumor response is modeled in this liver where a peripherally located left lobe tumor is perfused by intrahepatic collateral circulation after embolization of a parasitized extrahepatic artery (EHA) (right inferior phrenic artery). If all tumors responded positively (top), we interpreted this as evidence of successful distribution of microspheres through the collateral circulation. If asymmetric response was noted with inferior response in the tumor or part of the tumor perfused by collateral circulation (middle), we interpreted this as evidence of inadequate distribution of microspheres. If all tumors uniformly progressed (bottom), distribution of microspheres was not evaluable because even direct administration to the right lobe tumor via the hepatic artery did not result in therapeutic response, suggesting poor tumor biology and resistance to radioembolization.

Evaluation of Differential Territorial Tumor Response

Follow-up cross-sectional imaging by CT, MR imaging, or positron emission tomography (PET) was obtained on all surviving patients 2–3 months after treatment and approximately every 3 months thereafter. Individual tumor responses were measured by Response Evaluation Criteria In Solid Tumors (version 1.1) for CT and MR imaging, or European Organization for Research and Treatment of Cancer criteria for PET (9,10).

We specifically focused on measuring the objective response of tumors found in territories previously supplied by parasitized EHAs and compared the magnitude of change with the objective responses of tumors directly supplied by normal intrahepatic arteries. Uniform response (partial response, stable disease) was considered as evi-

dence of successful distribution of radioembolic microspheres via intrahepatic collateral vessels (Fig. 2). Heterogeneous response with inferior response in a territory previously supplied by a parasitized EHA was considered evidence of unsuccessful delivery of radioembolic microspheres to this territory. If all tumors uniformly progressed, distribution of microspheres could not be evaluated because even direct administration via the hepatic artery did not result in therapeutic response, suggesting poor tumor biology and resistance to radioembolization. In the absence of histopathology, this evaluation of differential territorial tumor response served as a surrogate to reflect the intrahepatic distribution of microspheres delivered to normal and to parasitized territories.

RESULTS

Identification and Embolization of Parasitized Extrahepatic Arteries

We detected 73 parasitized EHAs in 35 patients (17.4% of all patients). All identified parasitized EHAs perfused tumor territories large enough to be characterized by selective DSA or C-arm CT or both. Patients with parasitized EHAs included 15 men and 20 women with ages ranging from 22–76 years. There were 16 (45.7%) patients with primary hepatic malignancy and 19 (54.3%) with metastatic disease (Table 1). More than half of the patients received whole-liver treatment because they had diffuse bilobar disease. Most patients underwent single-session whole-liver treatment to limit the potential possibility for tumor progression in an untreated lobe and to minimize reimbursement issues.

Of 35 patients, 20 (57.1%) had only one parasitized artery, whereas 15 (42.9%) had more than one, with up to nine arteries identified (Table 2). Women showed a higher incidence of formation of parasitized EHAs compared with men (23.8% vs 12.8%, $P = .043$). Parasitization was most frequently detected in patients with hepatocellular carcinoma (30% of all patients with hepatocellular carcinoma) and metastatic neuroendocrine carcinoma (37% of all patients with metastatic neuroendocrine carcinoma). Other cell types, including metastatic ocular and cutaneous melanoma and ovarian epithelial and granulosa cell tumors, also parasitized EHAs, but only a few patients were treated for each of these histologies. The presence of parasitized EHAs was not associated with prior chemoembolization ($P = .123$); hepatic resection ($P = .608$); systemic chemotherapy ($P = .258$); antiangiogenic therapy with bevacizumab, sorafenib, or sunitinib ($P = .749$); or targeted anti–epidermal growth factor receptor therapy with cetuximab or panitumumab ($P = .397$). In 29 (82.9%) patients, tumors were located in segment VII, and all tumors were > 2 cm in diameter.

Embolization was successfully performed in all 73 identified parasitized EHAs in attempts to reestablish intrahepatic arterial supply to the parasitizing tumors. These included 29 (39.7%) right inferior phrenic arteries, 26 (35.5%) posterior intercostal arteries, 6 (8.2%) left inferior phrenic arteries, 5 (6.8%) right middle and inferior adrenal arteries, 4 (5.5%) greater omental arteries, 2 (2.7%) left internal mammary arteries, and 1 (1.4%) right internal mammary artery (Table 2 and Fig 3).

Table 1. Demographics and Treatment Details of Patients with Parasitized Extrahepatic Arteries (EHAs)

Demographics			
Age			
Mean 59.5 y (range 22–76 y)			
Sex			
Male 15, female 20			
Tumor Type		**Total (n = 35)**	**%**
Primary		16	45.7
Hepatocellular carcinoma	12		
Cholangiocarcinoma	4		
Metastatic		19	54.3
Neuroendocrine	10		
Colorectal	4		
Melanoma (ocular)	2		
Melanoma (cutaneous)	1		
Ovarian (epithelial)	1		
Ovarian (granulosa cell)	1		
Type of Radioembolization Microsphere Used		**No. EHA Patients**	
SIR-Spheres		23	
TheraSphere			12
Territory of Liver Treatment		**SIR-Spheres**	**TheraSphere**
Whole liver		19	
Single administration	14		
Two lobar administrations, different sessions	5		
Right lobe only		1	10
Right lobe and segment IV		3	2

Embolization of parasitized EHAs was well tolerated clinically. All patients undergoing phrenic artery embolizations noted discomfort referred to the ipsilateral shoulder during the embolization procedure; this usually dissipated within an hour. Only one patient had persistent symptoms, with self-limited moderate right-sided and small left-sided pleural effusion after embolization of a large right inferior phrenic artery; this regressed within 6 weeks of follow-up. No angiographic evidence of systemic-to-pulmonary venous shunting was found in any of the parasitized EHAs.

Evaluation of Intrahepatic Reperfusion

We were unable to evaluate the intrahepatic perfusion response in 9 patients by scintigraphy because the parasitized EHAs were discovered only at the time of microsphere administration, long after scintigraphy was performed; these patients were excluded from the scintigraphic analy-

Table 2. Anatomy of Parasitized Extrahepatic Arteries (EHAs)

No. Parasitized EHAs Identified per Patient	n	%
1 artery	20	57.1
2 arteries	5	14.3
3 arteries	3	8.6
4 arteries	5	14.3
> 4 arteries	2	5.7
Distribution of Parasitized EHAs per Patient	**n = 35 Total Patients**	**%**
Inferior phrenic only		
Right	18	51.4
Left	3	8.6
Right inferior phrenic and right intercostals	6	17.1
Right inferior phrenic and right middle and/or inferior adrenal	3	8.6
Right intercostals only	1	2.9
Right intercostals and right inferior adrenal	1	2.9
Left internal mammary	1	2.9
Greater omental	1	2.9
Bilateral inferior phrenic, right intercostals, bilateral internal mammary, and greater omental	1	2.9
Total Parasitized EHAs Identified	**n = 73 Total Arteries**	**%**
Inferior phrenic, including accessory arteries		
Right	29	39.7
Left	6	8.2
Right intercostal		
T8	2	2.7
T9	6	8.2
T10	8	11
T11	5	6.8
T12	5	6.8
Right middle and inferior adrenal	5	6.8
Greater omental	4	5.5
Internal mammary		
Left	2	2.7
Right	1	1.4

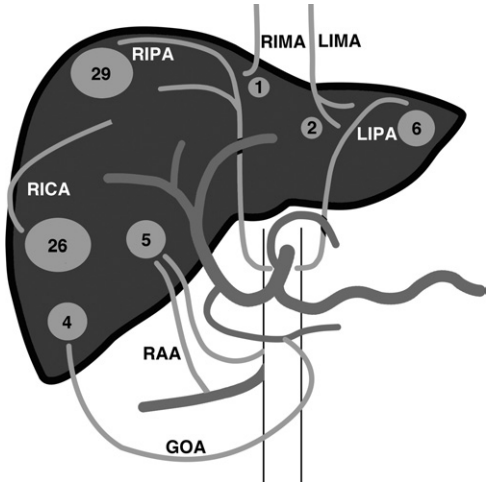


Figure 3. Distribution of parasitized extrahepatic arteries (EHAs) on which embolization was performed for reestablishment of intrahepatic perfusion to tumors is shown in light gray. Embolization of arteries was performed with large particles followed by coils to discourage additional parasitization from extrahepatic sources and to encourage reestablishment of intrahepatic arterial supply to tumors. Parasitized EHAs on which embolization was performed included right intercostal arteries (RICA), right and left inferior phrenic arteries (RIPA, LIPA), right and left internal mammary arteries (RIMA, LIMA), right middle and inferior adrenal arteries (RAA), and greater omental arteries (GOA).

sis. Of the remaining 26 patients, scintigraphy confirmed reestablishment of intrahepatic perfusion to tumors previously fed by parasitized EHAs in 25 of 26 patients (96.2%) (**Fig 4a–g**).

Intrahepatic perfusion of tumors previously supplied by parasitized EHAs was also confirmed immediately by DSA in 31 (93.9%) of 33 patients and by C-arm CT in 32 (94.2%) of 34 patients (**Table 3**). One patient showed evidence of hypoperfusion of the territory previously supplied by a parasitized EHA by all three imaging modalities. However, follow-up revealed a uniform tumor response, suggesting adequate delivery of microspheres to the territory with suspected hypoperfusion; this probably reflected hypertrophy of intrahepatic collateral channels in the time interval between the consolidation procedure and the time of radioembolization treatment. Another patient showed a mixed perfusion pattern by DSA and by C-arm CT in which nine parasitized EHAs were treated with embolization. On follow-up imaging, uniform tumor response was shown in eight of nine hepatic territories previously supplied by parasitized EHAs. The single nonresponding tumor was located in a territory previously supplied by an omental artery, and embolization was performed by coils only. No particles were used because of the risk of reflux into adjacent branches feeding stomach and bowel. This tumor presumably recruited new EHAs rather than intrahepatic arterial supply. No tumors supplied by parasitized EHAs on which embolization was performed with both particles and coils were able to recruit new EHAs.

Follow-up Response

Adequate follow-up imaging was available for 25 of 35 patients. The other 10 patients did not undergo imaging because of death (n = 6), poor performance status (n = 3), or not yet reaching the 2- to 3-month follow-up interval (n = 1). Of the 25 patients with adequate imaging, 20 were followed by CT, 3 were followed by MR imaging, one was followed by PET, and one was followed by both CT and PET.

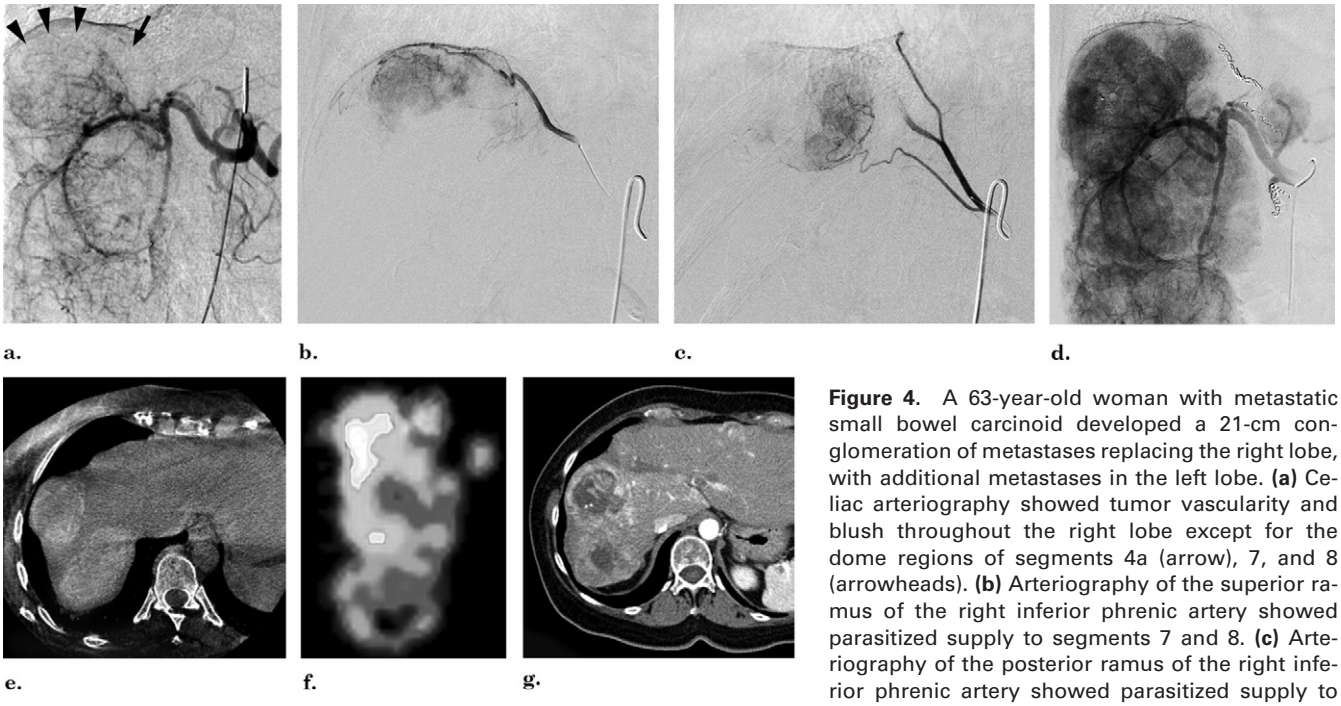


Figure 4. A 63-year-old woman with metastatic small bowel carcinoid developed a 21-cm conglomeration of metastases replacing the right lobe, with additional metastases in the left lobe. **(a)** Celiac arteriography showed tumor vascularity and blush throughout the right lobe except for the dome regions of segments 4a (arrow), 7, and 8 (arrowheads). **(b)** Arteriography of the superior ramus of the right inferior phrenic artery showed parasitized supply to segments 7 and 8. **(c)** Arteriography of the posterior ramus of the right inferior phrenic artery showed parasitized supply to segment 4a. Both rami were embolized with large particles (Embospheres 500–700 μm) followed by coils. **(d)** Proper hepatic arteriography after embolization showed new tumor blush in these regions, confirming reestablishment of intrahepatic supply to tumors previously supplied by parasitized EHAs. **(e)** Contrast-enhanced C-arm CT showed complete enhancement of all dome tumors. **(f)** Coronal single photon emission CT reconstruction of ^{99m}TcMAA scintigraphy confirmed deposition of radiotracer in these regions after injection in the proper hepatic artery. **(g)** Follow-up CT scan 3 months later showed extensive necrosis of dome tumors similar to that seen in other segments, suggesting successful delivery of radioembolic microspheres to regions previously supplied by parasitized EHAs.

Patients with parasitized EHAs tended to have advanced disease refractory to multiple therapies, and 8 of the 25 patients with adequate imaging follow-up showed uniform progressive disease in all hepatic territories, so distribution of microspheres could not be evaluated. After excluding patients with uniform progressive disease and patients with insufficient follow-up imaging, uniform partial response and stable disease responses were found in 16 (94.1%) patients with embolized parasitized EHAs, whereas 1 (5.9%) patient showed mixed tumor response in the hepatic territories previously supplied by parasitized EHAs (**Table 3**). Although few in number, these patients showed tumor responses supporting successful delivery of 30-μm microspheres to tumors through intrahepatic collateral channels after particle and coil embolization of parasitized EHAs. No patients showed evidence of nontarget radioembolization via retrograde flow in parasitized EHAs.

DISCUSSION

The goal of yttrium-90 radioembolization is to maximize deposition of beta radiation–emitting microspheres into intrahepatic neoplasms, while minimizing radiation exposure to normal hepatic parenchyma. However, considerable variability in the arterial supply to intrahepatic tumors may result in the actual dose administered to the target lesions being unpredictable and less than intended (5).

As is true in patients receiving chemoembolization treatment, tumors that receive arterial blood supply from parasitized EHAs are particularly at risk of being undertreated (8). The recognized risk factors increasing the likelihood of formation of parasitized EHAs include prior arterial therapies such as surgical ligation of the hepatic artery (11,12), chemoembolization (3), and hepatic arterial ported catheter placement (13). Other therapies such as surgical resection and conditions such as tumor rupture that may result in formation of adhesions between the liver and adjacent organs also increase the risk of forming parasitized EHAs (14). Certain anatomic characteristics of individual tumors are also recognized to increase the likelihood of forming parasitized EHAs, including large size, exophytic morphology, subcapsular location, and proximity to the bare area of the liver (3,8,15,16). Parasitized EHAs can develop even though the intrahepatic arterial supply remains intact (17,18). Even in the absence of intrahepatic neoplasm, collateral extrahepatic arterial supply to the liver may be shown after the hepatic artery or celiac artery has been ligated or occluded by embolization or thrombosis (11,12). These collateral routes can be portrayed both by CT angiography and by DSA during temporary balloon occlusion of the hepatic artery (7).

When parasitized EHAs are present in patients undergoing chemoembolization, these tumors may be treated directly by administration of chemoembolic material into

Table 3. Imaging and Tumor Response Evidence of Intrahepatic Reperfusion of Territories Previously Supplied by Parasitized Extrahepatic Arteries

	Successful Reperfusion of Territories via Intrahepatic Collateral Channels			
Perfusion of Territory Compared with Internal Control by Imaging Modality	**No. Patients**	**%**	**No. Arteries**	**%**
Digital subtraction angiography; 70 arteries in 33 patients studied				
Homogeneous	31	93.9	63	90.0
Hypoperfused	1	3.0	7	10.0
Mixed	1	3.0	—	—
C-arm computed tomography; 71 arteries in 34 patients studied				
Homogeneous	32	94.2	67	94.4
Hypoperfused	1	2.9	4	5.6
Mixed	1	2.9	—	—
^{99m}Tc-MAA single-photon emission computed tomography scintigraphy; 56 arteries in 26 patients studied				
Homogeneous	25	96.2	53	94.6
Hypoperfused	1	3.8	3	5.4
Mixed	0	0	—	—
Tumor Response (RECIST); 47 Arteries in 25 Patients Studied				
Evaluable disease (PR, SD)	17	68.0	36	76.6
Homogeneous response	16	94.1	35	97.2
Poor response	0	0	1	2.8
Mixed response	1	5.9	—	—
Uniform progressive disease (not evaluable for microsphere distribution)	8	32.0	11	23.4

PR = partial response; RECIST = Response Evaluation Criteria in Solid Tumors; stable disease = SD.

the parasitized EHAs, usually with acceptable rates of complications (3,14–20). However, the potential severity of complications resulting from nontarget radioembolization renders treatment through parasitized EHAs especially risky and, by convention, contraindicated. Administration of radioembolic microspheres into the phrenic artery carries the risks of diaphragmatic injury, radiation pneumonitis from intercommunication with the pulmonary arterial circulation, and diffuse systemic radioembolization from systemic venous-to-pulmonary venous shunting. We found a safe method to deliver radioactive microspheres to hepatic tumors perfused by parasitized EHAs by eliminating parasitic perfusion and restoring intrahepatic arterial supply.

Our earliest attempts to eliminate perfusion from parasitized EHAs using coils alone had limited success and frequently resulted in recruitment of additional extrahepatic parasitized arteries (eg, from adjacent intercostal arteries after coil embolization of the main intercostal parasitized EHA). The addition of using large particles eliminated this pitfall and may have helped to prevent retrograde flow from the intrahepatic vessels into the parasitized EHAs, which could have led to nontarget radioembolization.

It could be argued that bland embolization of the parasitized EHAs using particles could also be therapeutic in itself by causing ischemia, and such embolization is routinely performed in certain circumstances to treat neoplasms. However, the tumors in our study had more than one blood supply. Elimination of parasitized EHAs did not devascularize the tumors, as proven by continued enhancement with contrast agent on DSA and C-arm CT and uptake on scintigraphy. Using large-sized particles evidently prevented them from reaching the capillary level and did not render the tumors ischemic.

A limitation of our study involves the lack of histopathologic proof of successful delivery of microspheres to tumors previously supplied by parasitized EHAs. We have instead used the best available surrogate metrics of contrast enhancement, scintigraphic simulation, and tumor response. Although intrahepatic collateral vessels perfusing tumors previously supplied by parasitized EHAs can be shown by contrast-enhanced DSA and C-arm CT, the ability of these collateral vessels to allow free passage of the 30-μm microspheres cannot be assumed. Soluble contrast medium molecules are 5 orders of magnitude smaller than microspheres (21). More accurate simulation may be performed using ^{99m}TcMAA particles (size range 30–90 μm), but up to 10% of the particles measure < 10 μm in diameter, which could lead to overestimation of success of intrahepatic perfusion if collateral channels are < 30 μm in diameter (22). Perhaps the most compelling evidence of successful delivery of microspheres is radiographic evidence of tumor response. However, the advanced stage diseases treated resulted in some patients never undergoing follow-up imaging, others showing inexorable tumor progression, and only 17 patients with adequate imaging follow-up to support successful microsphere delivery. Our findings need to

be confirmed in larger series. In addition, many patients underwent adjuvant systemic therapy after radioembolization, which could partially mask poor microsphere distribution.

In conclusion, we found that embolization of parasitized EHAs supplying peripherally located hepatic tumors using coils and large particles allowed immediate reestablishment of intrahepatic arterial perfusion through collateral channels. These channels were apparently large enough to allow passage of radioembolic microspheres, enabling safe and effective radioembolization treatment of all tumors via the main hepatic arteries.

ACKNOWLEDGMENT

The authors thank Dr. A. K. Hosni for expert statistical advice.

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INVITED COMMENTARY

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Radioembolization continues to establish its role in the treatment of liver malignancies. Since its introduction into clinical care in 2001, the percutaneous approach has been established as preferred method, with hundreds of hospitals worldwide offering this novel treatment. The development has been controlled, with confirmation of safety, publication of methodology reports, and promising outcomes for a wide variety of tumor types; this has led to several consensus statements, research documents, and large-scale clinical trials (1–3). Specific to this modality is the need for meticulous angiography; this has been critical to a persistently good safety profile and continued adoption of yttrium-90 (4,5). The recognition of complex feeding vessels and anomalous vasculature to

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R.S. serves as a paid consultant for Sirtex Medical (Lane Cove, Australia) and MDS Nordion (Ottawa, Ontario, Canada), and has received funding for research from MDS Nordion.

J Vasc Interv Radiol 2011; 22:1362–1363

DOI: 10.1016/j.jvir.2011.07.013