Advancements in minimally invasive image-guided liver therapies

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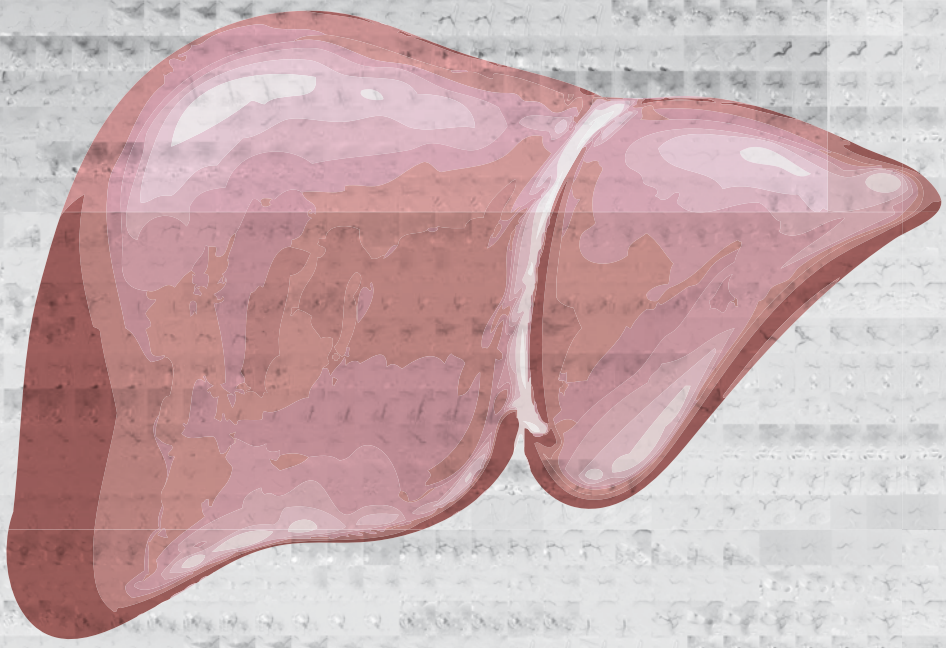
Chapter 6

Radioembolization with infusion of Y90 microspheres into a right inferior phrenic artery with hepatic tumor supply is feasible and safe



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ABSTRACT

Purpose

To evaluate the feasibility and safety of yttrium-90 (Y90) radioembolization through the inferior phrenic arteries (IPAs).

Methods

Retrospective analysis of 108 patients referred for radioembolization to treat primary (n=103) or secondary (n=5) liver malignancy was performed. Five patients had their hepatic malignant tumors supplied by the IPA and met the inclusion criteria for infusion of Y90 spheres into the IPA. DSA, catheter-directed computer tomography hepatic angiography (CTHA) and technetium-99m macroaggregated albumin (Tc-99m MAA) SPECT/CT were used to plan treatment. Bremsstrahlung SPECT/CT was performed 1 day after radioembolization. Follow-up included clinical and biochemical tests and cross-sectional CT or MRI.

Results

Parasitized extra-hepatic arteries were detected in 37.0% (n=40) of patients. Of these, 62.5% (n=25) had tumor supply through an IPA. Of the patients with IPA supply, 20% (n=5) underwent infusion of Y90 into the right IPA. Reasons for disqualifying patients for infusion into the IPA were less than 10% tumor supply (n=11), failed catheterization of IPA (n=3), arterioportovenous shunt (n=2), failed identification of IPA at pre-treatment angiography (n=1), and gastric or esophageal enhancement on CTHA (n=3). In all 5 patients technical success was demonstrated on Y90 imaging, with no significant extra-hepatic radionuclide activity. No adverse events related to IPA radioembolization occurred at mean follow-up of 4.5 months (range 2.2-10.1 months).

Conclusions

Delivery of Y90 microspheres through the right IPA is feasible and safe with the use of CTHA in addition to DSA and Tc-99m MAA SPECT/CT in patients with tumors with greater than 10% IPA supply.

INTRODUCTION

Radioembolization with yttrium-90 (Y90) microspheres is an effective treatment for patients with unresectable primary and secondary liver malignancy (1, 2). Microspheres are delivered to the hepatic tumors by selective hepatic arterial infusion. The infused microspheres lodge permanently within the vascular bed of the tumor to deliver high-energy ß-radiation (3). As each microsphere has a limited therapeutic range (mean tissue range 2.5mm; maximum 11mm), adequate deposition of microspheres throughout the entire tumorous region is essential to achieve optimal treatment results. This may be difficult or impossible to achieve in patients with tumors supplied by parasitized extra-hepatic arteries (PEAs). Unfortunately, 17-30.8% of patient with liver malignancies may have tumor supply through PEAs (4-7). The inferior phrenic arteries (IPAs) are responsible for the extra-hepatic supply in the vast majority of cases (4,6,8). Infusion of Y90 into the IPAs is generally considered not to be feasible because of the risks of non-target radiation injury (6,9).

We hypothesized that selective radioembolization into the IPAs is feasible and safe in selected patients when using a combination of digital subtraction angiography (DSA), catheter-directed computed tomography hepatic angiography (CTHA) and technetium-99m macroaggregated albumin (Tc-99m MAA) single photon emission computed tomography with integrated low-dose computed tomography (SPECT/CT) to plan and guide treatment. We retrospectively reviewed the feasibility and safety of infusion of Y90 microspheres directly into the IPAs.

METHODS

Approval by the Institutional Review Board (IRB) of our institution was obtained for this retrospective study.

Patients

We retrospectively reviewed reports and images of all pre-treatment and treatment angiograms performed between May 2010 and December 2011. In this period, pre-treatment angiography with Tc-99m MAA injections were performed in 108 patients for the following indications: hepatocellular carcinoma (HCC) in 99 patients (91.7%), metastasis from colorectal carcinoma in 4 patients (3.7%), cholangiocarcinoma in 2 patients (1.9%), hepatic angiosarcoma in 2 patients (1.9%) and metastasis from adrenocortical carcinoma in 1 patient (0.9%). Patient age ranged from 36-85 years (mean, 63.1 years) and 90 patients were male.

Among the 108 patients, 81 patients (75.0%) proceeded to have at least one treatment session with radioembolization. Seven patients underwent a second radioembolization treatment during the study period. All radioembolization procedures were performed with Y90 resin microspheres with a diameter of 20-60 μm (SIR-Spheres®, Sirtex Medical Limited, New South Wales, Australia).

Pre-treatment angiography and Tc-99m MAA

In all patients cross-sectional images obtained with either computed tomography (CT) and/or magnetic resonance imaging (MRI) were available and reviewed before the procedure. The angiographic protocol included selective DSA from the superior mesenteric artery, the celiac axis and hepatic arteries. All patients underwent CTHA using a hybrid 16-slice CT/angiography system (Toshiba, Tokyo, Japan). Selective inferior phrenic DSA and CTHA were performed in cases where tumor supply from the IPAs was suspected based on the pre-procedural cross-sectional imaging or if incomplete tumor enhancement was seen on DSA and/or CTHA from the hepatic arteries.

Selective DSA of the IPA was performed with a 5F Cobra catheter (Terumo, Tokyo, Japan) or 4F Sidewinder catheter (Terumo or Cordis, Miami Lakes, FL, USA). Subsequently, a 2.2F or 2.7F Progreat catheter (Terumo) was introduced co-axially through the 4F/5F catheter and DSA and CTHA were performed. CTHA from the IPA was performed using an injection rate of 1-3 ml/sec. The injected contrast volume for CTHA was calculated by adding the scan delay and scan time and multiplying the sum by the flowrate, with the scan delay being the time between the start of injection and enhancement of the region of interest at angiography.

Patients underwent standard coil embolization of hepaticoenteric anastomoses either on the day of the pre-treatment angiography or the day of radioembolizaton. In patients in whom radioembolization from the IPA was considered, angiography and CTHA images were carefully reviewed to identify the presence of IPA branches such as inferior vena cava, adrenal, esophageal, gastric and diaphragmatic arteries. If feasible, coil embolization of such arteries was performed with 0.018-inch coils (2mm Figure-8 or 3mm Diamond-shaped VortX, Boston Scientific, Natick, Massachusetts, USA).

At the end of the procedure, CTHA images were reviewed to visually estimate the contribution to tumor perfusion for each supplying artery as a percentage of total tumor perfusion. The Tc-99m MAA (total 5mCi in 3ml; particle size of 10-90μm) was then divided into corresponding portions and slowly hand-injected into each supplying artery. For the IPA, the injected volume of Tc-99m MAA ranged between 0.5-1ml (0.8-1.7mCi). All patients underwent Tc-99m MAA planar scintigraphy and SPECT/CT using a hybrid

SPECT/CT scanner (Philips Precedence, Amsterdam, Netherlands) for calculation of liver-to-lung shunt fraction and tumor-to-normal liver ratio and to exclude any non-target extrahepatic shunting of Tc-99m MAA. Predictive radiation dosimetry was performed by Medical Internal Radiation Dose (MIRD) macrodosimetry (ie, 'partition model').

Infusion of microspheres into IPA

Before infusion of Y90 microspheres, hepatic angiography and CTHA were repeated. Moderate enhancement of the adrenal gland or IVC was not considered to be a contra-indication for infusion of Y90 microspheres into the IPA. The activity of Y90 microspheres injected into the IPA was determined by Tc-99m MAA SPECT/CT predictive dosimetry, in accordance with target tissue masses determined by CT volumetry guided by CTHA of the IPA. Y90 microspheres were manually infused until the entire calculated dose was delivered or angiographic stasis was reached.

Safety assessment and follow-up

All patients underwent Y90 imaging one day after radioembolization. Y90 imaging of the abdomen was performed by bremsstrahlung SPECT/CT alone or in combination with Y90 internal pair production time-of-flight (TOF) positron emission tomography with integrated CT (PET/CT) as part of an unrelated research project. Also, planar liver-to-lung bremsstrahlung scintigraphy was performed. Special attention was paid to Y90 activity in the tumor area supplied by the IPA versus the rest of the tumor. Liver and renal function tests were routinely performed before discharge for all patients. Follow-up cross-sectional imaging by CT or MRI was routinely planned 3 months after treatment and approximately every 3 months thereafter. Adverse effects were classified into grade 1 to 5 in accordance with the common terminology criteria for adverse events version 3.0 (CTCAE v3) (10).

RESULTS

Identification of PEAs

Vascular tumor supply through PEAs was detected in 40 of 108 patients (37.0%) who underwent preparatory hepatic angiography with Tc-99m MAA injection. Of these 40 patients, 37 (92.5%) had HCC. Most patients (65.0%) were found to have only one PEA (Table 1). A total of 71 PEAs were detected. The IPAs were the most common source of extra-hepatic blood supply, seen in 38% of all PEAs (Table 1). Twenty-five patients (62.5% of patients with PEAs) had blood supply through one or both IPAs.

Table 1. Parasitized extra-hepatic arteries (PEAs): number per patient and types

Number of PEAs per patient	n (total = 40)	%
1 artery	26	65.0
2 arteries	8	20.0
>2 arteries	6	15.0

Identified PEAs	n (total = 71)	%
Inferior phrenic	27	38.0
Right	21	29.6
Left	6	8.5
Right middle and/or inferior adrenal	7	9.9
Pancreaticoduodenal arcade	6	8.5
Right renal capsular	6	8.5
Right gastro-epiploic	5	7.0
Cystic	4	5.6
Right gastric	4	5.6
Gastroduodenal branch	3	4.2
Superior mesenteric branch	3	4.2
Intercostal	2	2.8
Superior phrenic	1	1.4
Supraduodenal	1	1.4
Left gastroepiploic	1	1.4
Splenic artery branch	1	1.4

Parasitized extra-hepatic supply through the IPA

The demographics of the 25 patients with tumor supply through an IPA are given in Table 2. The mean maximum diameter of liver tumors supplied by the IPA was 13.5cm (range 5.8- 20.0 cm). Tumor supply through the right IPA was detected in 19 of the 25 patients (76.0%), through the left IPA in four patients (16.0%) and through both the right and left IPA in two patients (8.0%). Five patients with right IPA supply (26.3%) had a right liver lobe tumor with extension to the diaphragm, three (15.8%) had tumor extension to the bare area, and 11 (57.9%) had tumor extending to both the diaphragm and the bare area. All patients with left or bilateral IPA supply had a liver tumor extending to both the diaphragm and the bare area. In 11 (44.0%) patients there was vascular tumor supply through at least one other PEA in addition to the IPA supply.

Treatment IPA

In 17 of the 25 patients with blood supply through one or both IPAs (68.0%), the option of infusion of radioactive microspheres through the IPA was rejected without performing CTHA from the IPA (Table 3). The feasibility of performing radioembolization from

Table 2. Demographics patients with inferior phrenic artery (IPA) supply (n=25)

Characteristic	Value	
Age	mean 62.4 yrs	
	range 39-83 yrs	
Sex	n (total =25)	%
Male	22	
Female	3	
Tumor type	n	%
HCC	25	100
Tumor distribution	n	%
Bilobar	16	64.0
Unilobar	9	
Child-Pugh score	n	%
A	20	80.0
B	5	20.0
Vascular invasion	16	64%
Lymph node metastasis	2	8%
Distant metastasis	0	0%
BCLC stage		
A	7	28.0%
B	2	8.0%
C	16	64%

BCLC stage = Barcelona Clinic Liver Cancer staging system, HCC = hepatocellular carcinoma

the IPA was not further evaluated in these patients because of IPA supply less than 10% (n=11), failed catheterization of the IPA (n=3), arterioportovenous shunting (n=2), or failed identification of the IPA supply at the time of pre-treatment angiography (n=1). Eight patients did undergo CTHA from the IPA to evaluate the safety of microsphere infusion into the IPA.

In three of the eight patients who underwent CTHA from the IPA, Y90 microspheres infusion into the IPA was not considered safe based on imaging findings and Tc-99m MAA was therefore not injected into the IPA. In one patient, CTHA from the left IPA showed marked gastric enhancement through several small IPA branches. There was also tumor supply seen through the right IPA, but this was estimated to be less than 10% of the overall tumor

burden. Transarterial embolization (TAE) of both the right and left IPA was performed using 250-355 µm polyvinyl alcohol (PVA) particles (Contour; Boston Scientific) in the same setting as radioembolization through the hepatic arteries. In another patient, CTHA from the right IPA showed a small area of esophageal enhancement and marked enhancement of the right adrenal gland. In the third patient, reflux with enhancement of the adrenal glands and esophagus was seen at catheter-directed cross-sectional imaging from the right IPA. In the second and third patients, coil embolization of the IPA was performed in order to re-establish intrahepatic antegrade flow to the tumor area supplied by the IPA. Yet, in both patients we failed to demonstrate satisfactory re-establishment of flow

Table 3. Tumor characteristics, IPA supply and treatment of IPA territory

Parameter	Value		
Diameter of tumor with IPA supply	Mean 13.5cm (range 5.8 to 20.0 cm)		
Location of tumor supplied by IPA	n (total =25)		%
In contact with diaphragm	5		20.0
Bare area	3		12.0
In contact with diaphragm and bare area	17		68.0
Area supplied by IPA			
<10% of entire tumor volume	11		44%
10-20%	7		28.0%
20-30%	4		16.0%
30-40%	3		12.0%
Treatment IPA territory per patient	n (total =25)	% (of total)	Rationale not to attempt RE through IPA
No treatment	15	60.0%	
	11	44.0%	<10% supply
	3	12.0%	Failed catheterization IPA
	1	4.0%	Large APV shunt
TACE	1	4.0%	IPA supply not identified at preparatory DSA. Disqualified from RE because of lung shunt
TAE	2	8.0%	
	1	4.0%	Shunt IPA to PV
	1	4.0%	Gastric enhancement on CCTA
Coil-embolization	2	8.0%	
	2	8.0%	Esophageal enhancement on CCTA
Radioembolization	5	20%	

RE = radioembolization; TACE = trans-arterial chemo-embolisation; TAE = transarterial embolisation; PV = portal vein; CCTA = catheter-directed computer tomography angiography

through intra-hepatic collaterals to the IPA territory using DSA, CTHA and SPECT/CT. In five of the 25 patients (20%), Y90 microspheres were infused directly into the right IPA.

Infusion of Y90 microspheres into the IPA

Y90 microspheres were infused into the right IPA in all five cases with radioembolization through the hepatic arteries in the same session. Two patients had been treated with radioembolization once before, but without infusion of microspheres into the IPA. In one patient, the IPA supply was not identified during the first treatment. The other patient had undergone treatment twice with conventional TACE prior to the first radioembolization. Uncomplicated TACE had been performed from the right IPA during the second TACE session.

All 5 patients had large hypervascular right liver lobe tumors (mean diameter 18.2 cm; range 15.1-20.0 cm). Selective angiography and CTHA showed good forward flow and absence of reflux in all 5 cases. The mean activity of Y90 microspheres infused into the IPA was 0.6 GBq (range 0.3-0.8 GBq). In three patients (60.0%), coil embolization was

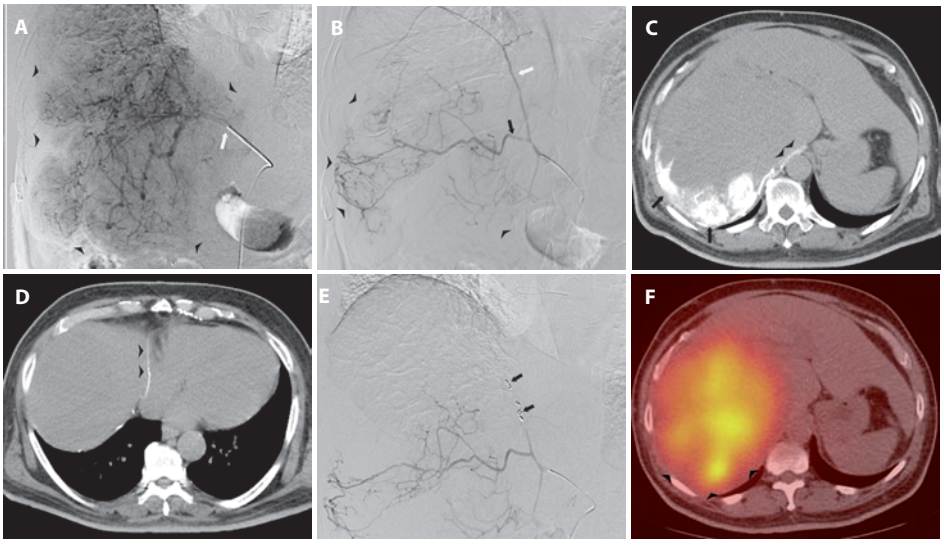

Figure 1. Images from a 64-year-old male with a large HCC. (a) DSA from the right hepatic artery (RHA) (white arrow) shows enhancement tumor (arrowheads). CTHA from the RHA showed absent enhancement of the posterior portion of the tumor (not shown). (b) DSA from the right IPA shows tumor supply (arrowheads) through the descending branch of the IPA (black arrow) and no obvious tumor supply from the ascending IPA branch (white arrow). (c+d). CTHA from the IPA shows enhancement of the posterior portion of the tumor (arrows) and the diaphragmatic crus (arrowheads) (c). The ascending IPA branch (arrowheads) does not supply the tumor (d). (e) Coils (black arrows) have been placed in the ascending IPA branch before infusion of Y90 microspheres into the RHA and right IPA. (f) Bremsstralung scan shows Y90 activity in the entire tumor, including the IPA territory (arrowheads).

performed of a diaphragmatic branch that was shown to supply the diaphragm and no tumor (Figure 1).

In one of the five patients, a small adrenal artery with tumor supply was seen to originate from the right IPA branch (Figure 2). TAE of this adrenal artery was performed with 150-250 µm PVA particles (Contour, Boston Scientific, Natick, MA, USA), and Y90 microspheres were infused into the IPA from a more distal position. In three of the five patients

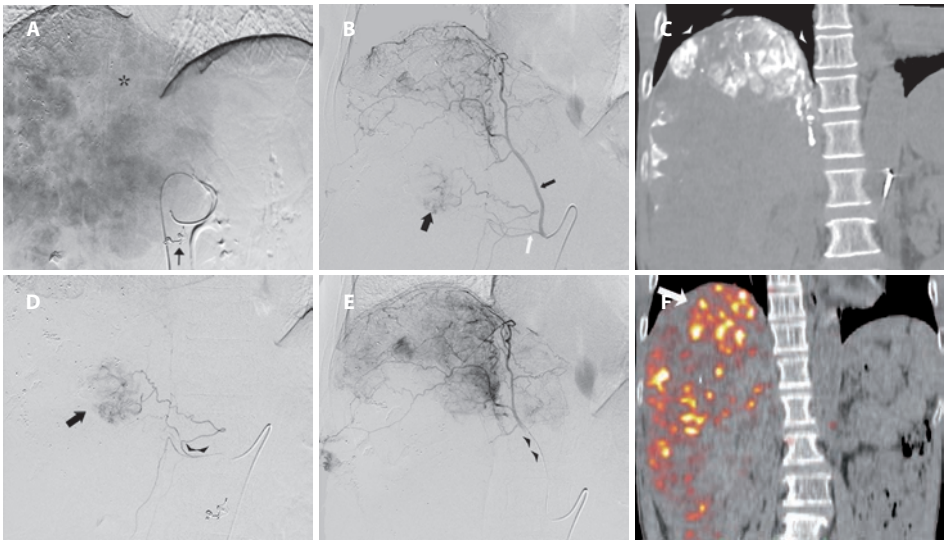

Figure 2. Images from 52-year-old male with a HCC in segment 4, 5, 6, 7 and 8. (a) DSA from the proper hepatic artery shows the large hypervascular tumor. Poor enhancement of the cranio-medial area is seen (asterix). Embolization of the gastroduodenal artery and right gastric artery has been performed with respectively an Amplatzer vascular plug 4 and microcoils (black arrow). (b) DSA from the right IPA (small black arrow) shows enhancement of the cranial portion of the tumor and supply to a small tumor area (large black arrow) through a proximal adrenal artery branch (white arrow). (c). CTHA from the IPA shows enhancement of the cranial tumor part (arrowheads). (d) DSA from the adrenal artery through a microcatheter (arrowheads) shows the small area of tumor enhancement (arrow). The adrenal artery was embolized using PVA particles. (e) After placement of the microcatheter (arrowheads) more distally into the IPA, Y90 microspheres were infused. This was followed by infusion into the proper hepatic artery. (f) PET/CT performed 1 day after radioembolization shows higher Y90 activity in the IPA territory (arrow) compared to the rest of the tumor.

(60.0%), CTHA from the IPA showed mild to moderate enhancement of the right adrenal gland. In 2 patients (40.0%) moderate enhancement of the IVC was seen in addition to this.

Y90 activity in IPA territory

All five patients who underwent infusion of microspheres into the IPA showed Y90 activity in the IPA territory on bremsstralung SPECT/CT. In three patients, homogenous activity was seen in the entire IPA territory. In the patient who underwent TAE of the adrenal artery, the small area supplied by this artery did not show Y90 activity. In another patient there was good Y90 activity in the medial portion of the IPA territory, but unsatisfactory activity in the lateral portion. Before infusion of microspheres, TAE of a right renal capsular artery was performed with 355-500 μm PVA particles (Contour, Boston Scientific). This capsular artery also showed competing supply to the lateral area of the IPA territory and the lack of Y90 activity was thought to be a result of the TAE.

Safety of radioembolization into IPA

One of the five patients who underwent radioembolization into the IPA developed a small puncture site hematoma during the procedure. No other intra-procedural complications were encountered in these five patients. In all five patients radioembolization was performed under local anesthesia and none of the patients required additional administration of analgesics during or after the procedure.

The mean follow-up duration for the five patients was 4.5 months (range, 2.2-10.1 months). One patient who had come from overseas for medical treatment in our institution was lost to follow-up. He was well at the time of discharge from the hospital and returned to his home country 7 days after radioembolization. None of the patients developed adverse effects attributable to radioembolization into the IPA.

DISCUSSION

Radioembolization through PEAs is generally considered to be contraindicated because of the high risk of non-target radiation (6,9). Unfortunately, up to 30.8% of patients with a hepatic malignancy will have vascular tumor supply through one or more PEAs (4-7). In our study, 37.0% of patients had one or more PEAs supplying part of their hepatic neoplasms. The IPAs are the most frequent source of extrahepatic collateral blood supply to hepatic tumors (4-6,8). In the present study, 62.5% of patients with PEAs had tumor supply through one or both IPAs. Particular risk factors for parasitized supply through the IPAs are a tumor location in the bare area and contact of the tumor with the diaphragm (11).

The right and left IPA divide into an ascending and descending branch and give rise to superior suprarenal and middle suprarenal branches. The right IPA may give rise to

arteries to the IVC, whereas the left IPA can give rise to accessory splenic, gastric and esophageal branches (11, 12). Potentially, the IPA can communicate with systemic arteries such as the internal mammary, intercostal, musculophrenic and pericardiophrenic arteries (12,13). Transpleural intercommunication with the pulmonary arteries can also exist, usually in patients with underlying chronic lung inflammation (14).

Administration of Y90 microspheres into the IPAs has been deemed unsafe because of the potential risks of radiation injury to the diaphragm and adrenal glands (6,9). In addition to this, spheres that are infusion into the right IPA could theoretically find their way through branches supplying the IVC, causing radiation injury to the IVC. Infusion of Y90 into the left IPA could theoretically result in radiation injury to the spleen, stomach or distal esophagus. In addition, reflux could occur into the communicating systemic arteries or into the vessel from which the IPA originates. Patients with intercommunication of the IPA and pulmonary vessels are at risk of radiation pneumonitis or even diffuse systemic irradiation if the microspheres shunt into the pulmonary veins (6).

Different strategies can be adopted in patients with PEAs. TAE and TACE have been successfully performed through different PEAs, although TACE from the IPA may be complicated by pleural effusion and atelectasis (7,11,15-22). Although TAE and TACE are feasible treatments to address parts of the hepatic malignancy supplied by PEAs, they are not the preferred option. Those patients that are assessed to undergo radioembolization, often have been selected either because of disease progression after TACE or a contra-indication to TACE such as portal vein embolization. Another option to address parasitized extra-hepatic supply was recently reported by Abdelmaksoud et al. in a study including 35 patients with 73 PEAs (6). Prior to Y90 microspheres infusion, the authors attempted to eliminate parasitic perfusion and restore intrahepatic blood supply to liver tumors by embolizing the PEAs with large particles and coils. After this method had been employed, successful re-establishment of antegrade flow through intra-hepatic collateral vessels into tumor areas previously supplied by PEAs was confirmed by both DSA and C-arm CT in 94% of territories and by scintigraphy in 96%. They also observed symmetric regional tumor response in 94% of patients and this was inferred as successfully delivery of microspheres to the territories previously supplied by PEAs. The method of embolization of PEAs offers an important advantage, as the risk of nontarget radiation is substantially lower when Y90 microspheres are infused into the hepatic arteries instead of into a PEA. However, there are uncertainties with regards to the approach of coilembolization. In the study of Abdelmaksoud et al., there was no histological confirmation of successful delivery of microspheres in the areas supplied by the PEAs. Only surrogates to measure microspheres implantation were used, such as contrast enhancement, Tc-99m MAA uptake, and tumor response. Furthermore, many patients

in the study by Abdelmaksoud et al. had also received adjuvant systemic therapy after radioembolization. Tumor response may therefore not only be a result of successful implantation of Y90 microspheres in the PEA territories. The biggest disadvantage of the method of embolizing the PEAs is that the success of microspheres delivery to the PEA territories remains unpredictable and accurate predictive radiation dosimetry for the PEA territories is therefore difficult.

In our study, five patients underwent radioembolization with direct infusion into the IPA. In all 5 cases infusion of microspheres was performed from the right IPA. None of the five patients experienced serious adverse events at a mean follow-up of 4.5 months. The use of CTHA was considered to be crucial in selecting patients for radioembolization via the IPA. CTHA provides the necessary complementary information to DSA with better image quality and spatial resolution than cone-beam CT and Tc-99m MAA scintigraphy. Furthermore, CTHA enables the vascular territory of a particular artery to be accurately delineated. Artery-specific CT volumetry guided by CTHA achieves accurate tissue mass estimates for improved radiation dosimetry to the IPA territory – a current practice at our institution (23).

Limitations of our study are the retrospective nature and the small number of patients. Further studies are needed to confirm the safety of infusion of radioactive microspheres into the IPA.

In conclusion, this study shows that the delivery of beta-emitting microspheres through the right IPA is feasible and safe in selected patients. The use of CTHA in addition to DSA and Tc-99m MAA scintigraphy is crucial in minimizing the risk of non-target radiation injury. The study does not support any conclusions on the infusion of Y90 microspheres into the left IPA or other PEAs. The risk of radiation injury to the esophagus or stomach is likely to be significantly higher when infusion of spheres would be performed from the left IPA versus the right IPA.

REFERENCES

1. Sangro B, Salem R, Kennedy A, Coldwell D, Wasan H. Radioembolization for Hepatocellular Carcinoma: A Review of the Evidence and Treatment Recommendations. Am J Clin Oncol 2011; 34:422-43.
2. Salem R, Thurston KG. Radioembolization with Y90ttrium Microspheres: A State-of-the-Art Brachytherapy Treatment for Primary and Secondary Liver Malignancies. Part 1: Technical and Methodologic Considerations. J Vasc Interv Radiol 2006; 17:1251-1278.
3. Murthy R, Nunez R, Szklaruk J, et al. Yttrium-90 Microsphere Therapy for Hepatic Malignancy: Devices, Indications, Technical Considerations, and Potential Complications. RadioGraphics 2005; 25:S41–S55.
4. Miyayama S, Matsui O, Taki K, et al. Extrahepatic Blood Supply to Hepatocellular Carcinoma: Angiographic demonstration and Transcatheter Arterial Chemoembolization. Cardiovasc Intervent Radiol 2006; 29:39–48.
5. Chung JW, Kim HC, Yoon JH, et al. Transcatheter arterial chemoembolization of hepatocellular carcinoma: prevalence and causative factors of extrahepatic collateral arteries in 479 patients. Korean J Radiol 2006; 7:257–266.
6. Abdelmaksoud MHK, Louie JD, Kothary N, et al. Embolization of Parasitized Extrahepatic Arteries to Reestablish Intrahepatic Arterial Supply to Tumors before Yttrium-90 Radioembolization. J Vasc Interv Radiol 2011; 22:1355-1362.
7. Miyayama S, Yamashiro M, Okuda M, et al. The March of Extrahepatic Collaterals: Analysis of Blood Supply to Hepatocellular Carcinoma Located in the Bare Area of the Liver After Chemoembolization. Cardiovasc Intervent Radiol 2006; 29:39–48.
8. Kim HC, Chung JW, Lee W, Jae HJ, Park JH. Recognizing extrahepatic collateral vessels that supply hepatocellular carcinoma to avoid complications of transcatheter arterial chemoembolization. Radiographics 2005; 25:S25–S39.
9. Riaz A, Lewandowski RJ, Kulik LM, et al. Complications following radioembolization with yttrium-90 microspheres: a comprehensive literature review. J Vasc Interv Radiol 2009; 20:1121–1130.
10. Trotti A, Colevas AD, Setser A, et al. CTCAE v3.0: development of a comprehensive grading system for the adverse effects of cancer treatment. Semin Radiat Oncol 2003; 13:176–181.
11. Gwon DI, Ko GY, Yoon HK, et al. Inferior Phrenic Artery: Anatomy, Variations, Pathologic Conditions, and Interventional Management. Radiographics 2007; 27:687–705.
12. Loukas M, Hullett J, Wagner T. Clinical anatomy of the inferior phrenic artery. Clin Anat 2005; 18 (5):357-365.
13. Webb WR, Jacobs RP. Transpleural abdominal systemic artery-pulmonary artery anastomosis in patients with chronic pulmonary infection. Am J Roentgenol 1977; 129:233-236.
14. Do KH, Goo JM, Im JG, Kim KW, Chung JW, Park JH. Systemic Arterial Supply to the Lungs in Adults: Spiral CT Findings. Radiographics 2001; 21:387–402.
15. Soo CS, Chuang VP, Wallace S, Charnsangavej C, Carrasco H. Treatment of hepatic neoplasm through extrahepatic collaterals. Radiology 1983; 147:45–49.
16. Kim JH, Chung JW, Han JK, Park JH, Choi BI, Han MC. Transcatheter arterial embolization of the internal mammary artery in hepatocellular carcinoma. J Vasc Interv Radiol 1995; 6:71–77.
17. Duprat G, Charnsangavej C, Wallace S, Carrasco CH. Inferior phrenic artery

embolization in the treatment of hepatic neoplasms. Acta Radiol 1988; 29:427–429

18. Kodama Y, Shimizu T, Endo H, et al. Spontaneous rupture of hepatocellular carcinoma supplied by the right renal capsular artery treated by transcatheter arterial embolization. Cardiovasc Intervent Radiol 2002; 25:137–140.
19. Miyayama S, Matsui O, Nishida H, et al. Transcatheter arterial chemoembolization for unresectable hepatocellular carcinoma fed by the cystic artery. J Vasc Interv Radiol 2003; 14:1155–1161.
20. Miyayama S, Matsui O, Taki K, et al. Transcatheter arterial chemoembolization for hepatocellular carcinoma fed by the reconstructed inferior phrenic artery: Anatomical and technical analysis. J Vasc Interv Radiol 2004; 15:815–823.
21. Kim HC, Chung JW, An S, Seong NJ, Son KR, Jae HJ, Park JH. Transarterial chemoembolization of a colic branch of the superior mesenteric artery in patients with unresectable hepatocellular carcinoma. J Vasc Interv Radiol 2011; 22:47-54.
22. Tajima T, Honda H, Kuroiwa T, et al. Pulmonary complications after hepatic artery chemoembolization or infusion via the inferior phrenic artery for primary liver cancer. J Vasc Interv Radiol 2002; 13:893–900.
23. Kao YH, Tan EH, Burgmans MC et al. Image-guided personalized predictive dosimetry by artery-specific SPECT/CT partition modeling for safe and effective Y90 radioembolization. J Nucl Med. 2012; 53:1-10.