

Angiographic considerations in patients undergoing liver-directed radioembolization with ^{90}Y microspheres

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Abstract

Catheter-directed, transarterial internal brachytherapy, using ^{90}Y radioactive microspheres is gaining acceptance as a valuable treatment option in selected patients with liver malignancies. Knowledge of the radiological anatomy of the visceral arteries, including the variant anatomy of celiac trunk, superior mesenteric artery and end branches as well as technique and catheter skills for careful vessel occlusion prior to ^{90}Y delivery are of major importance to safely and efficiently treat patients with radioembolization. In this review article, normal vascular anatomy, common variants and influence of tumors on the feeding arteries will be discussed. Finally, techniques of pre-treatment vessel occlusion, technique of ^{90}Y -administration and the added value of C-arm computed tomography during work-up and administration of radioactive microspheres will be described. (*Acta gastroenterol. belg.*, 2010, 73, 489-496).

Key words : liver, interventional procedure, tumor, embolization.

Introduction

Regional, minimally invasive treatment modalities are becoming more and more effective in the treatment of primary and secondary liver tumors. Both, percutaneous techniques, like percutaneous ethanol injection (PEI), radiofrequency ablation (RFA) or cryoablation and endovascular techniques like transarterial chemoembolization or transarterial chemoinfusion have demonstrated some clinical benefit in selected patients (1,2).

Recently a new type of endovascular technique, transcatheter radioembolization, has been introduced into the clinic for the treatment of patients with primary or secondary liver tumors (3,4,5). Radioembolization can be considered as a form of intra-arterial brachytherapy, where microspheres, impregnated with the radio-active isotope yttrium-90 (^{90}Y) are infused through a small catheter into the hepatic arteries and finally occluding the distal arterioles of the tumor (6). These nonbiodegradable microspheres, consisting of glass (Therasphere, MDS Nordion, Ottawa, Canada) or resin (SIR-spheres, Sirtex Medical Ltd, Lane Cove, Australia) have a diameter of 20-35 μm . The most important difference between glass and resin microspheres is the activity in each microsphere : the resin-based microspheres all contain 50 Becquerel (Bq), the glass-based microspheres each contain 2500 Bq. The standard activity vial is 3 GBq ; corresponding to 1.2 and 40-80 million microspheres for respectively the glass-based and resin-based

microspheres. ^{90}Y is a pure beta-emitter and decays to stable Zirconium-90 (^{90}Zr) with a physical half-life of 64 hours. The average energy of the beta particles is 0.9367 MeV with a mean tissue penetration of 2.5 mm and a maximum penetration of 10 mm (7,8).

Angiographic work-up prior to ^{90}Y administration

Once a patient is selected for transcatheter radioembolization, an angiographic evaluation of the visceral arteries is performed in order to document the visceral arterial anatomy, potential anatomic variants, potential extrahepatic arteries totally or partly feeding the tumor. Additionally, extrahepatic vessels originating from the hepatic arteries have to be occluded in order to isolate the hepatic circulation, thereby infusing the ^{90}Y -microspheres into the hepatic tumor(s) and avoiding delivery of radioactive microspheres into the gastrointestinal tract parenchyma.

Evaluation of visceral vascular anatomy including normal and variant anatomy

Visceral angiographic evaluation starts by performing selective catheterisation of the celiac trunk and the superior mesenteric artery. The conventional, normal anatomy of the celiac trunk, defined as Michels type I, demonstrates the three major endbranches : splenic artery, left gastric artery and the common hepatic artery. Further, the common hepatic artery gives off the proper hepatic artery and the gastroduodenal artery ; the proper hepatic artery continues as the right hepatic artery, giving off the left hepatic artery. The right hepatic artery splits into anterior and posterior branches ; the left hepatic artery feeds segments II and III. Liver segment IV is fed by branches originating from both right and left hepatic artery and sometimes from the proper hepatic artery. However, according to Michels *et al.* (9), this anatomy is present in only 55% of subjects ; in the remaining 45%,

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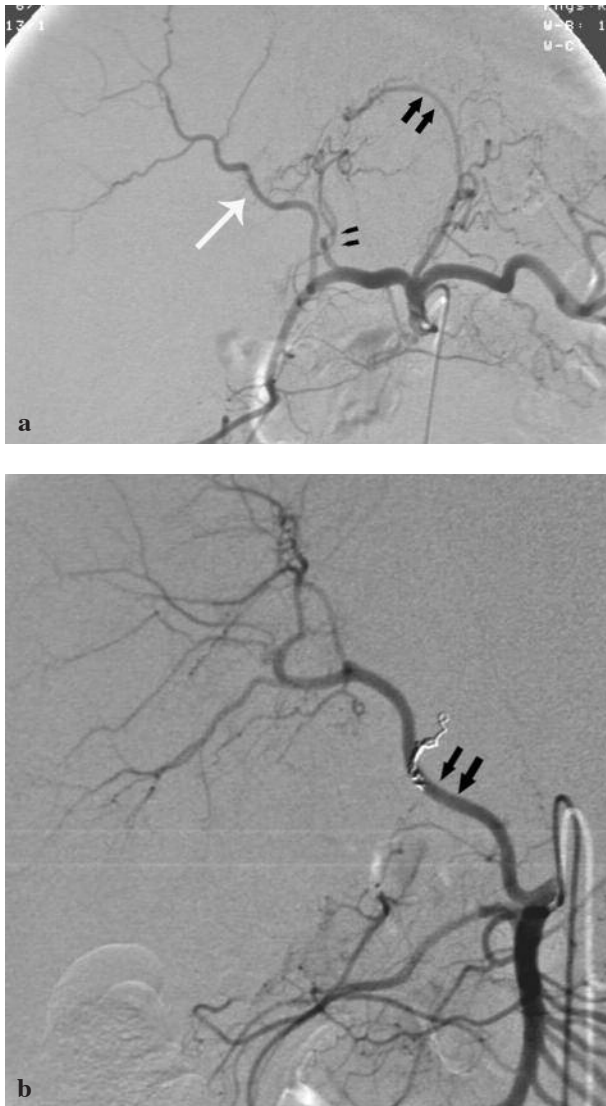


Fig. 1. — Variant hepatic artery anatomy : (a) selective injection of the celiac trunk depicts the left hepatic artery (black arrows), originating from the left gastric artery ; an accessory hepatic artery feeding liver segment 4 (black arrowheads) and the right hepatic artery (white arrow), partly feeding the right liver lobe – (b) Selective injection of the superior mesenteric artery shows an accessory right hepatic artery (black arrows), originating postostially from the superior mesenteric artery main branch.

an anatomic variant will be present. The most common variants of the hepatic arterial anatomy are described by Michels *et al.* (9) and divided in 10 types, including a left replaced hepatic artery (10%), originating from the left gastric artery, a right replaced hepatic artery (11%), originating from the superior mesenteric artery and an accessory right (7%) and left (8%) hepatic artery respectively originating from the left gastric and superior mesenteric artery (Fig. 1). Other, less common variants can be demonstrated in less than 5% of cases (Fig. 2).

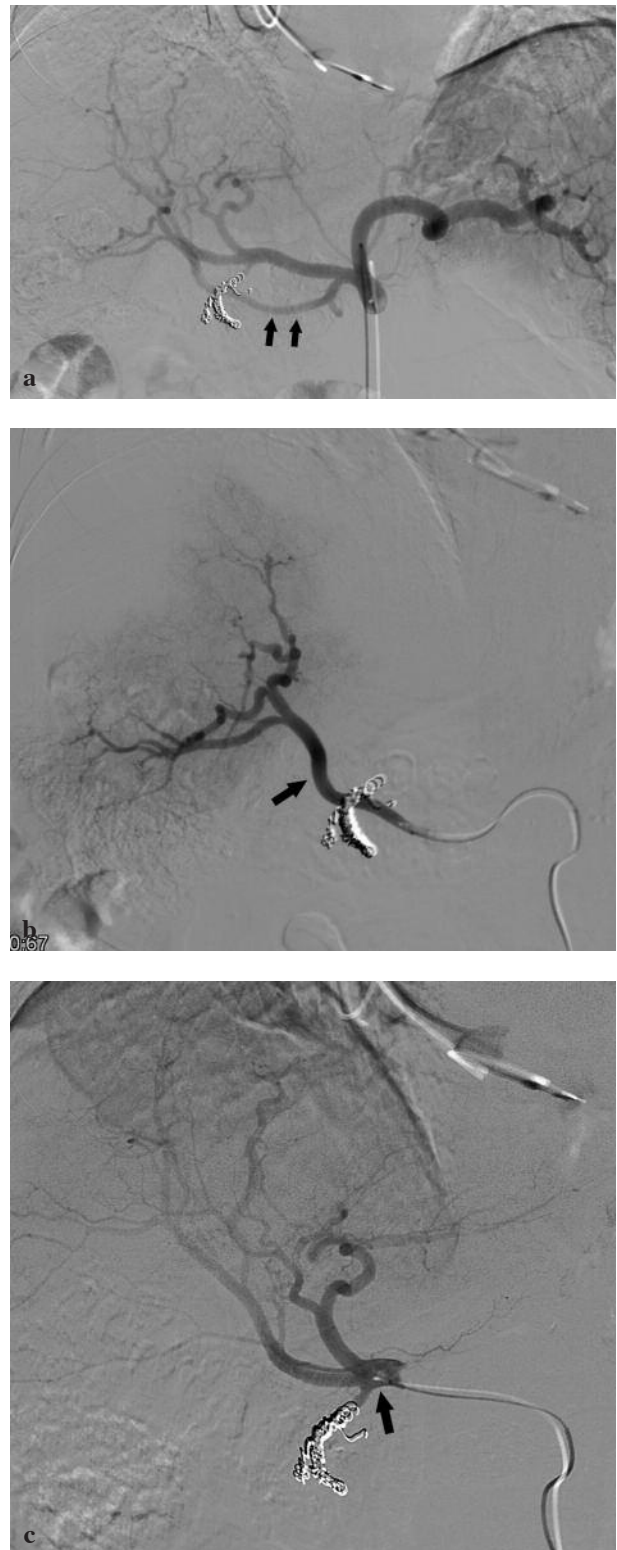


Fig. 2a-b-c. — Uncommon variant hepatic artery anatomy : (a) Selective injection of the celiac trunk reveals an accessory right hepatic artery (arrows), originating from the proximal common hepatic artery – (b) Selective injection of this accessory right hepatic artery (arrow) demonstrates the end branches feeding a part of the right liver lobe – (c) Selective injection of the proper hepatic artery (arrow) shows the trifurcation of the left hepatic artery, the right hepatic artery and the coiled gastroduodenal artery.

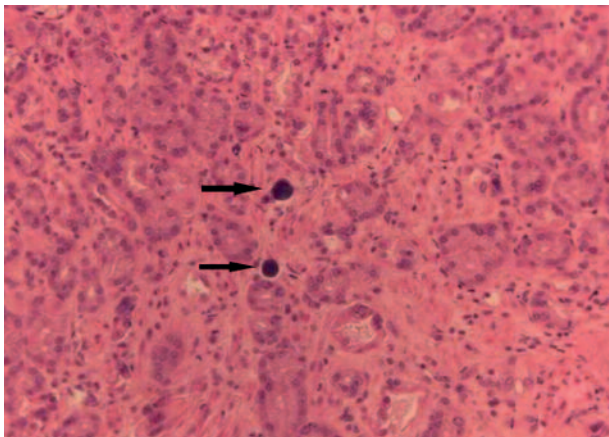


Fig. 3. — Detail of corpus-type gastric mucosa with 2 micro-spheres visible in blood vessels (black arrows) (Haematoxylin-Eosin stain, original magnification 400 x) – courtesy Prof. G. De Hertogh, Leuven, Belgium.

Which vessels to be occluded prior to ⁹⁰Y administration

During ⁹⁰Y-work-up, the hepatic arterial vasculature has to be isolated from extrahepatic vessels, originating from the hepatic arteries as infusion of radio-active microspheres into the gastrointestinal (GI) arteries invariably leads to severe gastritis, ulceration (Fig. 3) or even perforation and peritonitis (10-13). As opposed to peptic ulcers, radioembolization-induced GI-ulcers are caused from the serosal surface and thereby very difficult to heal despite adequate medical treatment. In some cases, surgical treatment can be required to treat these medication-resistant ulcers.

The largest extrahepatic vessel, originating from an hepatic artery, is the gastroduodenal artery (Fig. 4). The next most important extrahepatic vessel is the right gastric artery, most often originating from the proper or left hepatic artery (Fig. 5). The right gastric artery can make some macroscopic anastomoses with the left gastric artery. In case antegrade catheterisation and occlusion is technically not possible, retrograde catheterisation through the left gastric artery can be an option (Fig. 6). Other, less common extrahepatic arteries are the falciform artery, feeding the anterior abdominal wall (Fig. 7). Failure to identify or embolize this vessel can result in severe abdominal pain, peri-umbilical skin rash and skin necrosis.

The cystic artery, commonly originating from the right hepatic artery, is a point of discussion with regard to prophylactic embolization or not. The gallbladder is fed not only by the cystic artery, but also by collaterals or perforators from the hepatic parenchyma or even the gastroduodenal artery. Additionally, the incidence of radiation-induced cholecystitis is very low if no prior prophylaxis was performed ; in contrast, proximal coil-embolization of the cystic artery can also lead to



Fig. 4a-b-c. — (a) Selective injection of the celiac trunk shows a classic anatomy ; the non-hepatic vessels depicted are the gastroduodenal artery (white arrows) and the right gastric artery (black arrows) – (b) superselective catheterization of the gastroduodenal artery (white arrow) with use of a micro-catheter prior to coil-embolization – (c) Injection of contrast medium into the proper hepatic artery demonstrates proximal coil-occlusion (white arrows) of the gastroduodenal artery. Note partial opacification of the right gastric artery, originating from the proximal left hepatic artery (black arrows).

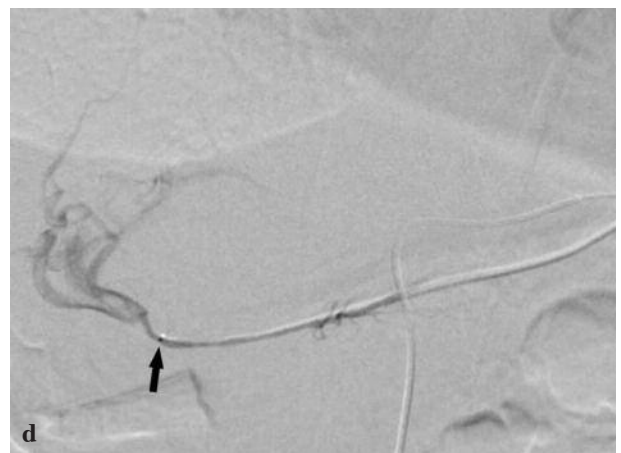
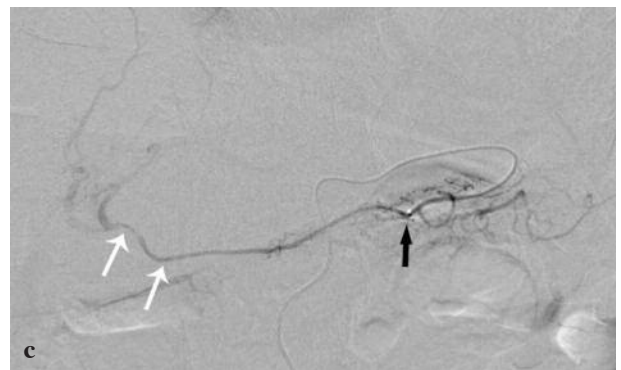


Fig. 5a-b. — (a) Superselective catheterization of the right gastric artery (black arrow), originating from the proximal left hepatic artery ; coils in the proximal gastroduodenal artery (white arrows) – (b) Control angiography after proximal coil-embolization (black arrow) shows absence of contrast medium in the right gastric artery end branches. Note also coils in the proximal gastroduodenal artery (white arrows).



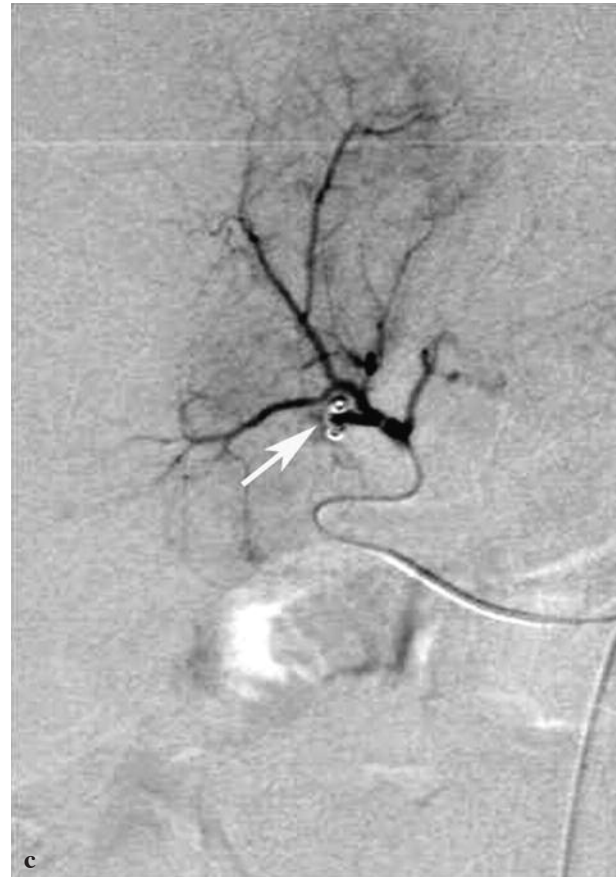
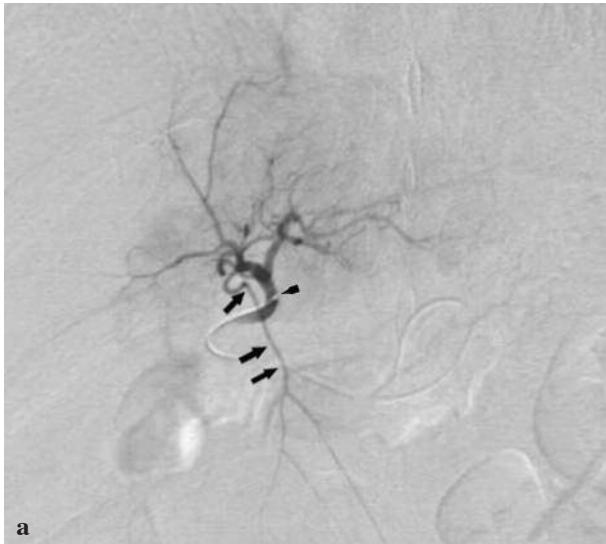


Fig. 7a-b-c. — (a) Selective injection of the left hepatic artery (arrowhead) opacifies a small branch projecting out of the liver area with end branches projecting in the umbilical area : falciform artery (arrows). (b) Superselective catheterization with use of a microcatheter clearly depict all extrahepatic end branches (arrows) of this artery. (c) Control angiography of the left hepatic artery after coil-embolization (white arrow) cannot demonstrate anymore the falciform artery.

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 Fig. 6a-b-c-d-e. — (a) Selective injection of the distal proper hepatic artery clearly reveals the right gastric artery (arrows) originating at the ostium of the left hepatic artery – (b) It was technically impossible to catheterize the right gastric artery ; therefore, the left gastric artery was catheterized (black arrow). (c) Through a left to right gastric artery anastomosis (black arrow), the right gastric artery (white arrows) could be cannulated retrogradely. (d) Once the tip of the microcatheter (arrow) was placed in the proximal part of the right gastric artery, coil-embolization was started. (e) Contrast injection in the left hepatic artery (black arrow) after coil-embolization (white arrows) could not show opacification anymore of the right gastric artery.

ischemic cholecystitis. In our practice, no routine prophylactic cystic artery coil-embolization is performed.

Technically, prophylactic vessel occlusion is routinely performed with use of a microcatheter and 0.018 inch microcoils (14), except for the occlusion of the gastroduodenal artery. This artery can also be occluded with use of large 0.035 inch coils or even with use of an Amplatzer vascular plug (15), both of these occlusion devices require an 0.038 inner lumen 4 or 5 French diagnostic catheter.

Flow redistribution of intrahepatic vessels : when and how ?

Based on a consensus among a multidisciplinary group of experts in the field of radioembolization, this new interventional technique should only be provided to the affected lobe or segment and in cases of bilateral lobar involvement, it should be provided as a single

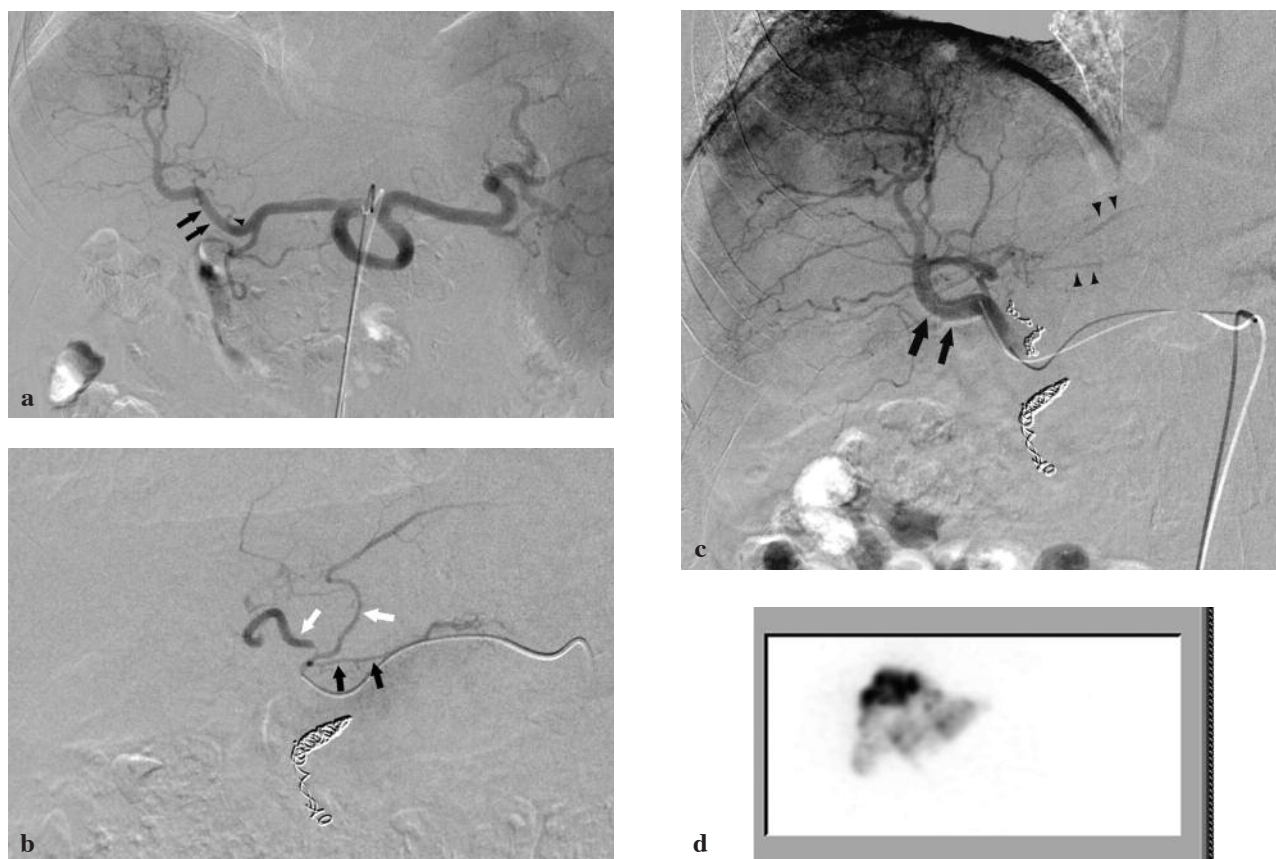


Fig. 8a-b-c-d. — (a) Selective catheterization of the celiac trunk in a patient with a multifocal hepatocellular carcinoma extending over both liver lobes. The right hepatic artery (arrows) is hypertrophic ; the left hepatic artery (arrowhead) is hypotrophic. (b) Selective catheterization of the left hepatic artery (white arrows) reveals opacification of the right gastric artery (black arrows). It was technically impossible to cannulate this artery with use of several microcatheter and micro-guidewires. (c) After coil-embolization of the proximal left hepatic artery, thereby bridging the ostium of the right gastric artery with microcoils, contrast injection into the right hepatic artery (black arrows) demonstrates opacification of end branches of the right and left hepatic artery (black arrows). The left hepatic artery end branches (arrowheads) are fed by collaterals communicating between the right and left hepatic artery. Note also the absence of opacification of the right gastric artery. (d) Macroaggregated albumin (MAA) scan after single injection of ^{99m}Tc in the right hepatic artery shows multifocal hotspots in both liver lobes : the macroaggregates also passed through the collaterals between the right and left liver lobe.

whole-liver infusion or as sequential unilobar sessions (16). However, in case of (complex) variant anatomy, one liver lobe can have two or more feeding arteries originating from different abdominal visceral trunks or two or more segmental vessels come from the right and left hepatic arteries. In order to inject safely and efficiently the ^{90}Y -microspheres, proximal coil-occlusion of one or more hepatic feeding arteries thereby allowing the infusion of the radioactive microspheres from one single or a maximum of two hepatic vessels could be considered (17). This technique of vascular redistribution, based on the existence of arterial collaterals between different hepatic segments and even lobes (18), has been performed with success prior to intra-arterial port catheter implantation in the proper hepatic artery and thereby treating the whole liver (19). Karunanithy and co-workers (20) recently demonstrated that the same technique of flow distribution prior to ^{90}Y infusion can

be performed with an effective treatment result in the previously coiled hepatic segment or lobe as demonstrated by both SPECT/CT after ^{99m}Tc infusion and PET/CT during follow-up after ^{90}Y administration (Fig. 8). These authors also argued that this technique of flow redistribution should not be performed in patients with hepatocellular carcinoma because of the propensity of such tumors to recruit collateral arterial supply from extrahepatic sources, especially as the tumors are located exophytically.

Finally, this technique of flow redistribution potentially can lead also to clinical problems if patients respond well to the treatment and become a candidate for surgery : if e.g. the left hepatic artery, originating from the left gastric artery, is coiled and subsequently, the patient becomes a candidate for right hemi-hepatectomy, the residual remnant liver would be devoid of direct arterial supply.

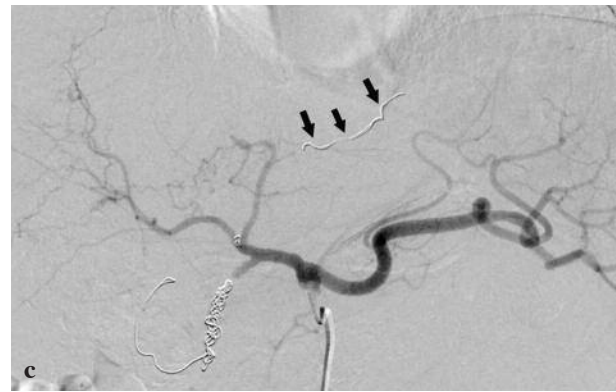
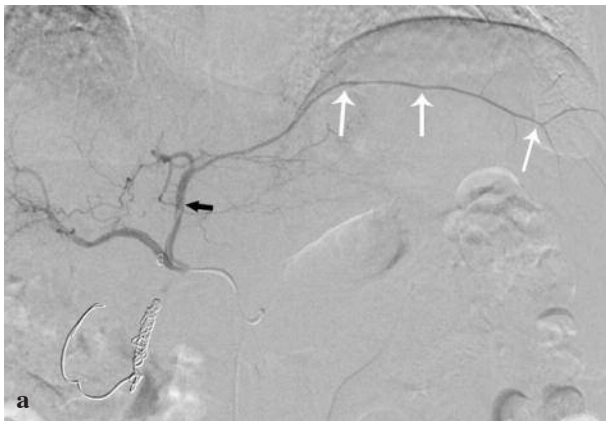


Fig. 9a-b-c. — Selective injection of contrast medium with the tip of the catheter located into the left hepatic artery (black arrow) depicts reflux into the right hepatic artery and clear opacification of the end branches of the left hepatic artery. One end branch (white arrows) projecting just below the left diaphragm seems to be a non-hepatic artery. (b) Cone beam CT after injection of contrast medium through the microcatheter in the left hepatic artery clearly shows the extrahepatic artery (white arrows) located at the level of the left diaphragm : the left inferior phrenic artery. (c) After proximal coil-embolization (black arrows), there was no more opacification of this non-hepatic artery.

Added value of C-arm computed tomography (CT) prior to radioembolization

Rotational C-arm computed tomography is a new radiological technology based on fast 200° rotation of the angiographic C-arm around the patient and thereby allowing reconstructed CT-like images in axial, coronal and sagittal projections. Images can be performed without contrast injection or during intravenous or intra-arterial contrast-injection. Several studies have demonstrated that C-arm CT during transcatheter injection of contrast medium can depict extrahepatic contrast enhancement, not detected by ^{99}Tc macroaggregated albumin (MAA) scanning (21) or incomplete tumor enhancement from one catheter tip position. Therefore, C-arm CT can affect the initial treatment plan, based on digital subtraction angiography and ^{99}Tc MAA scan in 25-33% of cases (21-24). Depiction of extrahepatic enhancement necessitates relocation of the catheter tip or additional coil-embolization and will avoid extrahepatic ^{90}Y delivery, potentially resulting in gastric ulcer or radiation-pancreatitis (Fig. 9).

What to do in case of excessive hepatopulmonary shunt ?

Hepatopulmonary shunt fraction exceeding 20% of ^{99}Tc MAA injected into the hepatic arteries during ^{90}Y

work-up is an absolute contra-indication to ^{90}Y radioembolization. In these cases alternative locoregional treatment options should be considered, like chemoembolization with or without drug-eluting beads or chemoinfusion. However, a few case reports describe the use of additional endovascular techniques to successfully reduce the hepatopulmonary shunt below 20% and in that way making radioembolization possible without clear risk of radiation pneumonitis. Rose *et al.* (25) performed chemoembolization with use of acrylated collagen embolic agents to reduce the shunt and Bester *et al.* (26) temporarily placed occlusion balloons in the hepatic veins during ^{90}Y delivery ; however, these additional techniques are not yet validated for safety or efficiency.

Conclusion

Liver-directed ^{90}Y radioembolization is a recently developed and promising interventional technique for the treatment of primary and secondary liver malignancies. However, multidisciplinary effort, including the disciplines of medical, surgical and radiation oncology, nuclear medicine and diagnostic and interventional radiology, is strictly required for safe and efficient work-up and treatment. The interventional radiologist plays a pivotal role in this management of patients treated by ^{90}Y microspheres : during angiographic work-up, complete

understanding of the vascular visceral anatomy is strictly needed ; a careful skeletonisation of the hepatic arteries, including coil-embolization of non-hepatic arteries as well as use of cone beam CT during angiography in selected case will lead to a safer and more efficient delivery of ⁹⁰Y microspheres into the liver tumors and eventually result in better clinical response as already demonstrated by a recently published randomised trial comparing conventional chemotherapy without or with addition of resin-based ⁹⁰Y radioembolization (5).

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