

# Yttrium-90 Radioembolization Mapping and Therapy

What to do and what to avoid.

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The use of minimally invasive procedures to manage primary and metastatic liver cancer has become increasingly common with the rising incidence of hepatic malignancies. Radioembolization, also known as *selective internal radiation therapy* or *radiation microsphere therapy*, is a complex yet minimally invasive procedure that aims to selectively deliver high doses of internal radiation using an intra-arterial infusion of microspheres loaded with the radionuclide yttrium-90 (Y-90).<sup>1,2</sup> Indications for Y-90 radioembolization include managing primary liver malignancies and metastatic disease of the hepatic parenchyma.<sup>3</sup> Patient selection criteria is covered in the literature, and some radioembolic agents of choice currently include SIR-Spheres Y-90 resin microspheres (Sirtex Medical Inc.) and glass TheraSpheres (BTG International Ltd.).<sup>4,5</sup>

## OVERVIEW

Radioembolization treatment is a two-stage outpatient process: the preparation/mapping stage and the treatment stage. In our institutions, patients are carefully evaluated, often incorporating multidisciplinary evaluation from medical oncology, surgical oncology, radiation oncology, transplant surgery, hepatology, and interventional radiology. After clinical evaluation by interventional radiology, appropriate patients are scheduled for an angiographic preradioembolization mapping procedure, with a treatment date preselected 7 to 10 days after the mapping procedure.

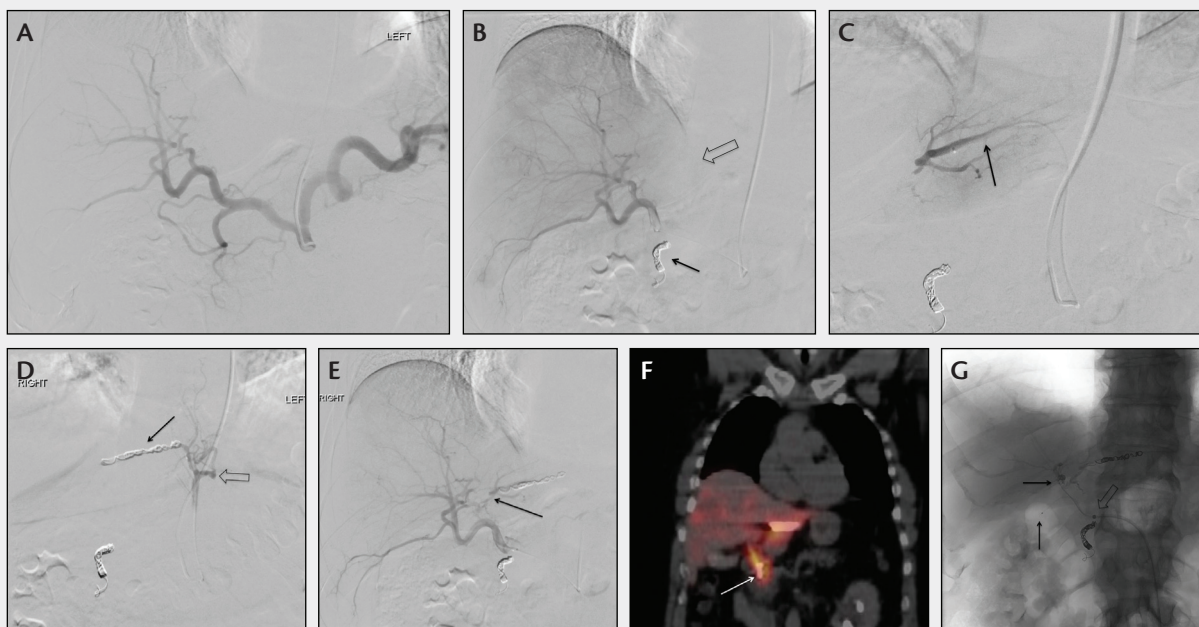
The mapping procedure serves two distinct purposes. First, delineation of the hepatic arterial anatomy is important for eventual dose delivery and to avoid

nontarget delivery. Variant hepatic arterial anatomy is common and occurs in up to 45% of patients (see Case Report 1).<sup>6</sup> Determining and isolating the hepatic arterial branches perfusing the tumor(s) can help avoid possible complications. In addition, this procedure may be used to exclude, by means of embolization, hepaticomesenteric collaterals.

Second, assessment of hepatopulmonary shunting is vital to determine the eventual radiation dose given to the patient.<sup>7</sup> The degree of shunting is estimated through intra-arterial infusion of technetium-99m-labeled macroaggregated albumin (Tc-99m MAA) (4–5 mCi) and subsequent measurement of the lung and liver activity.<sup>5</sup> Although presence of a hepatopulmonary shunt is not an absolute contraindication, the radiation dose to the lungs should not exceed 30 Gy in a single setting, and the cumulative dose to the lungs should not exceed 50 Gy. The MAA scan also helps identify potential extrahepatic uptake of Tc-99m MAA, and we routinely perform single photon emission computed tomography (SPECT)/CT rather than planar imaging because we prefer the extra anatomic detail it provides (as seen in Case Report 1).

We prefer to position the microcatheter in the same location between the mapping procedure and the treatment, as we believe the information provided by the MAA scan is the most accurate depiction of the subsequent treatment. After the treatment, it is standard practice to obtain a bremsstrahlung SPECT scan. We often do not obtain bremsstrahlung SPECT scan because it typically does not change the treatment and can extend the patient's time in the department. We routinely prescribe methylprednisolone and recommend continuation of a

# Case Report 1



**A:** A 55-year-old man with bilobar metastatic colorectal cancer. A digital subtraction angiogram of the celiac artery from a transradial approach using a 110-cm, 5-F Sarah catheter shows splenic and common hepatic arteries. The common hepatic artery divides into the gastroduodenal and proper hepatic arteries.

**B:** A selective microcatheter angiogram of the proper hepatic artery shows normal opacification of the right hepatic artery status after coil embolization of the GDA (straight arrow). The right gastric artery is not visualized; however, there is lack of opacification of the lateral segment of the left hepatic lobe (block arrow) raising suspicion of the presence of a replaced left hepatic artery from the left gastric artery (also known as a *gastrohepatic trunk*).

**C:** A superselective angiogram of the left gastric artery shows replaced left hepatic artery arising (straight arrow) with hepatic parenchymal opacification.

**D:** The decision was made to redistribute the flow of the left hepatic lobe to the proper hepatic artery. The replaced left hepatic artery origin was embolized (straight arrow), and selective left gastric arteriography shows opacification of gastric branches.

**E:** Subsequent superselective angiography from the proper hepatic artery shows coils in the replaced left hepatic artery with immediate redistribution of the left hepatic lobe arterial supply (straight arrow) from the proper hepatic artery. Tc-99m MAA was infused from this position to cover the whole liver.

**F:** Unexpectedly, although the subsequent SPECT/CT scan coronal reformat after Tc-99m MAA instillation shows coverage of the entire liver, there is significant deposition in the duodenum (white arrow). It was surmised that a supraduodenal artery branch was present, and it was not well visualized on the angiogram.

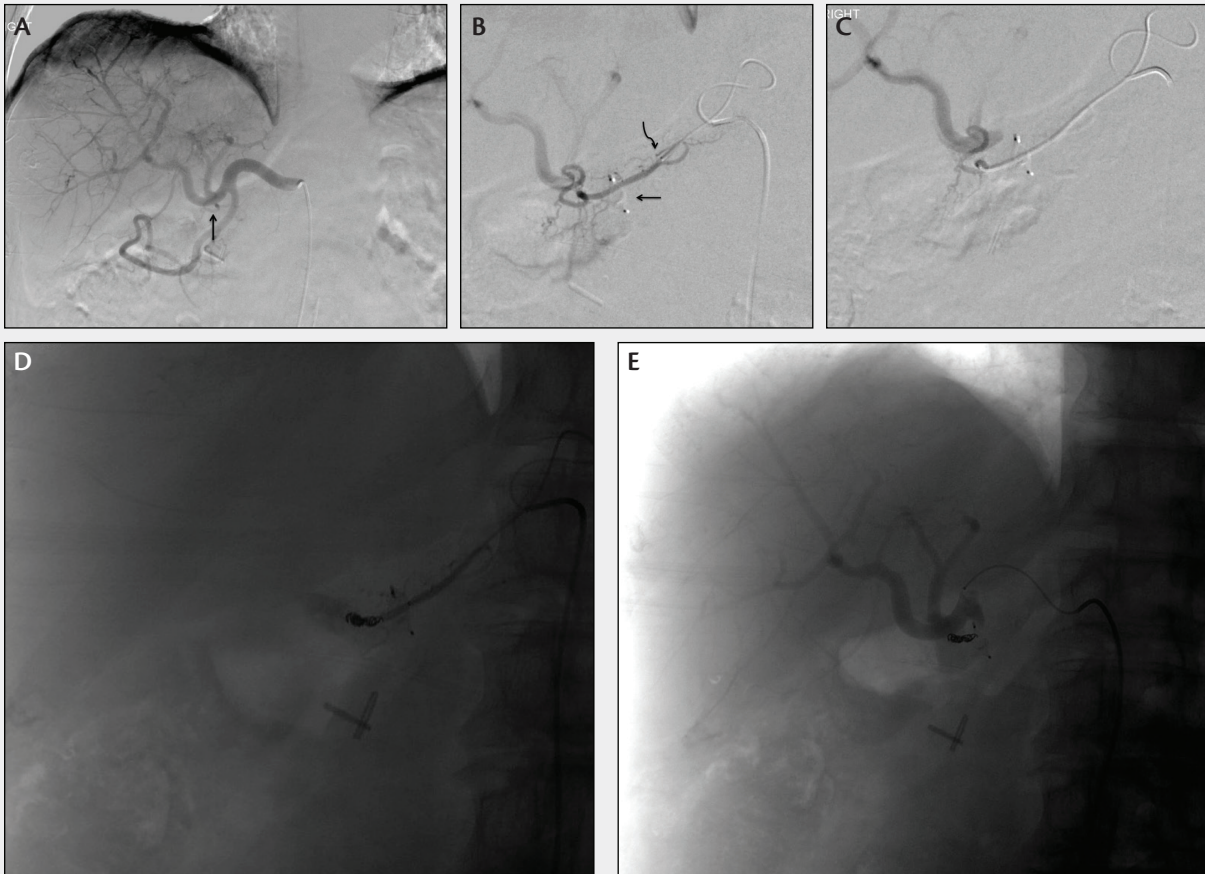
**G:** In order to avoid duodenal deposition, the decision was made to split the Y-90 treatment dose for administration. Nonsubtracted angiography performed during treatment shows a 6-F Ansel sheath (block arrow) from a femoral approach positioned in the common hepatic artery with two microcatheters positioned in the right and middle hepatic arteries (straight arrows). The lobar doses were administered in sequential fashion.

proton pump inhibitor for at least 1 month after the procedure. We do not routinely prescribe antibiotic prophylaxis for patients after the procedure. Patients are scheduled for a clinic visit and a 1- to 3-month follow-up MRI or CT angiogram (CTA) of the abdomen for primary hepatic malignancies versus a positron emission tomography/CT for metastatic tumors to assess response to therapy.

## MAPPING STUDY AND EMBOLIZATION

In our practice, we have predominantly shifted toward a transradial approach (TRA) to gain access to the abdominal aorta, although we still utilize a transfemoral approach as needed, and choice of access site tends to be operator dependent. We use a 5-F Glidesheath Slender (Terumo Interventional Systems) via the left radial artery. The

## Case Report 2



**A:** A 62-year-old woman with bilobar metastatic ocular melanoma. Digital subtraction angiography of the common hepatic artery shows conventional hepatic arterial anatomy with the presence of a right gastric artery arising from the left hepatic artery (arrow).

**B:** The GDA was subsequently embolized with a plug (straight arrow), and attempts to catheterize the right gastric artery were unsuccessful. Selective angiography of the left gastric artery (curved arrow) opacifies the right gastric artery origin through its collateralization and subsequently the right and left hepatic arteries.

**C:** The microcatheter tip was subsequently advanced to the right gastric artery via the left gastric artery connection, and angiography opacifies the right and left hepatic arteries from this position.

**D:** Coil embolization was then performed on the right gastric artery origin through the microcatheter placed from the left gastric artery.

**E:** Subsequent superselective microcatheter angiography from the proper hepatic artery shows no further filling of the right gastric artery or the GDA. Tc-99m MAA was infused from this position to cover the whole liver.

technical details of transradial access are discussed in the literature.<sup>8</sup> In most cases, a 110-cm Sarah, Jacky, or tiger Optitorque catheter (Terumo Interventional Systems) and a 1.5-mm J-Tip Glidewire (Terumo Interventional Systems) or Bentson guidewire (Cook Medical) are used to traverse the subclavian artery and advance into the abdominal aorta to select the mesenteric vessels. If difficulty accessing the descending aorta is encountered due to a tortuous

aortic arch, a 110-cm pigtail catheter and an exchange-length, angled, stiff Glidewire can almost always navigate the tortuosity, which is then exchanged for the mesenteric selective catheter. There is some hindrance to cone beam CT use with TRA, which may require a learning curve for the physicians and technologists, but complex embolization can routinely be done from this approach with the appropriate equipment.



Thorough angiography is necessary; however, we do not perform an aortography, because it is an unnecessary contrast dye load. All patients undergo cross-sectional imaging including a CTA or MRI of the abdomen, which should be studied carefully in advance. We always start with a superior mesenteric artery (SMA) arteriogram to assess for the presence of replaced or accessory hepatic arteries; however, a thin-cut CTA can delineate these vessels as well and can sometimes obviate the need for an SMA angiogram. The arteriogram is obtained at a rate of 4 to 6 mL/sec for 24 to 30 mL. This is allowed to extend into the venous phase to assess for patency of the portal vein. The celiac artery is then selectively catheterized to evaluate the hepatic arterial anatomy. A celiac arteriogram is obtained at rates of 4 to 5 mL/sec for 16 to 25 mL. If an SMA angiogram is not obtained, celiac angiography is performed in the venous phase to evaluate the portal vein. Subsequently, a 3-F microcatheter of choice (eg, Renegade Hi-Flo, Direxion [both Boston Scientific Corporation], or Progret [Terumo Interventional Systems]) is used to perform superselective angiography of the common, right, and left hepatic arteries. Angiography of the common hepatic artery is performed at a rate of 3 to 4 mL/sec for 12 to 16 mL, and angiography of the right and left hepatic arteries is performed at a rate of 2 to 3 mL/sec for up to 12 mL. A selective left gastric arteriogram may be considered to evaluate for replaced or accessory left hepatic arteries. Cone beam CT is used extensively in our practice to delineate the anatomy, including the arterial feeders for the tumor(s), and to assess treatment coverage of the liver.

Depending on the lesion location and the arteries identified via angiography, prophylactic embolization of the supraduodenal, gastroduodenal (GDA), right gastric, accessory gastric, falciform, or inferior phrenic arteries may be performed. We prefer not to embolize the cystic artery, even when identified in the treatment zone, as the incidence of radiation-induced cholecystitis is low. Embolization of the right gastric artery may be performed by entering via the left gastric artery when it cannot be catheterized from its hepatic origin (see Case Report 2). Embolization is accomplished with either detachable or nondetachable coils and plugs. We typically use a combination of these embolic agents. Use of high-flow microcatheters has been associated with difficulty deploying some detachable coils, and familiarity with which kinds of coils can and cannot easily deploy through a given microcatheter is extremely beneficial. We believe the benefits of a high-flow microcatheter, which provides better diagnostic angiograms with higher flow rates and better opacification, outweigh the drawbacks with coils.

Being mindful of which vessels the microspheres could reflux into often guides us to which vessel may require embolization. If the right hepatic artery is the target vessel and the first vessel the microspheres would reflux into is the left hepatic artery, embolization is typically not performed. Careful evaluation for the presence of the right gastric artery should be performed when infusing Y-90 in the left hepatic artery. If therapy is being infused from the proper hepatic artery, the GDA and right gastric artery likely need to be embolized. When embolizing the GDA, the key aspect is to ensure embolization over a long length and back up to the origin of the vessel to minimize chances of recanalization. We have also had instances of collateral formation from the distal hepatic arteries to the distal GDA when only the proximal portion of the GDA has been occluded. For this reason, we also do not embolize the GDA when we believe it is unnecessary, such as in a lobar treatment when the microcatheter can be placed distally, away from the GDA origin.<sup>9</sup> We often prefer starting with soft detachable coils distally, such as Concerto coils (Medtronic), to understand the optimal coil sizes and ensure more precise placement. This step may be followed by detachable Interlock (Boston Scientific Corporation) coils or pushable coils such as Tornado or Nester coils (both Cook Medical), which have more body and thrombogenicity. We then often use detachable coils again when approaching the origin of the vessel to prevent extension into the hepatic artery. Microvascular plugs, such as the MVP microvascular plug (Medtronic) and the Amplatzer Vascular Plug 4 (St. Jude Medical, Inc.), can also be used to embolize the GDA. The right gastric artery can be embolized with coils or a microvascular plug. Completion angiography performed after embolization should not show any further flow.

Small accessory left hepatic or right hepatic arteries may be embolized to redistribute perfusion to the native left or right hepatic artery for a single microcatheter administration. However, one should be wary of attempting intrahepatic redistribution of perfusion with segment IV or other intrahepatic lobar segments, as predicting whether the left or right hepatic artery will take over the perfusion in these situations can be difficult.

## LOBAR VERSUS WHOLE LIVER TREATMENT

In cases of primary hepatic malignancy, including hepatocellular carcinoma, we prefer segmental or lobar treatments, even with bilobar disease. As a result, the infusion microcatheter can be placed distally into either the right or left hepatic arteries. Lobar therapy often obviates the need for embolization of branch vessels

off the common hepatic artery. In cases of metastatic disease, particularly colorectal cancer, data from the SIRFLOX trial are based on whole liver Y-90 therapy.<sup>10</sup> Therefore, in metastatic disease with bilobar tumors, we perform both staged treatments (but mostly whole liver treatments), and this is dependent on operator preference. For metastatic neuroendocrine disease, given the side effects we have seen from tumor cell death and secretion of peptides and hormones, we still opt for lobar treatments in bilobar disease.

If there is challenging hepatic anatomy where an infusion cannot be performed from the proper hepatic artery safely, the Y-90 dose can be split between two separate microcatheters, which are placed distally into the hepatic lobes. This may be done with sequential treatments in the same setting using a 5-F catheter and microcatheter that are deposited in between treatments. Or, we often use a 6-F Flexor Check-Flo Introducer Ansel 2 guiding sheath (Cook Medical) into the ostium of the celiac artery from a transfemoral approach, followed by placement of two separate microcatheters deep into the right and left hepatic arteries so that each microcatheter can be infused temporally and then disposed of at once.

## OUTCOMES

Several studies have demonstrated radioembolization therapy to be safe and effective in the treatment of primary and metastatic hepatic malignancies.<sup>11</sup> Early analysis of a prospective cohort of 20 patients treated with Y-90 therapy reported significant outcomes with respect to both survival and quality of life.<sup>12</sup> Radioembolization has also been shown to be safe and effective in unresectable hepatocellular carcinoma, with 79% showing tumor response when percent reduction and/or tumor necrosis were used as a composite measure of tumor response.<sup>13</sup> With respect to metastatic disease from colorectal cancer, recent data from the landmark SIRFLOX trial demonstrated statistically significant median liver progression-free survival when Y-90 was used in conjunction with standard chemotherapy.<sup>14</sup> However, no improvement in overall progression-free survival was identified when compared to chemotherapy alone. Combination of data from the SIRFLOX trial and two other trials is being awaited to evaluate overall survival in a large cohort of patients. In metastatic neuroendocrine tumors, a review of available literature demonstrates safe and effective use of radioembolization in liver-dominant disease.<sup>15</sup>

## CONCLUSION

Selective internal radiation therapy has been shown to be an effective outpatient therapy for patients with

either primary hepatic malignancies or metastatic liver disease.<sup>11-15</sup> A thorough angiographic mapping study with embolization of some of the major branches of the common hepatic and proper hepatic arteries is a major component of the two-stage process for Y-90 therapy. Lobar or segmental therapy sometimes obviates the need for embolization in our recent experience; however, new users should be cautious, as the repercussions of nontarget delivery of Y-90 microspheres can be significant. ■

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