Multiple Arteries Supplying a Single Tumor Vascular Distribution: Microsphere Administration Options for the Interventional Radiologist Performing Radioembolization

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Radioembolization (RE) has become an increasingly common procedure for patients with liver-dominant primary liver tumors or metastatic disease. Results for RE are generally considered to be as favorable as transarterial chemoembolization (TACE), and may even be more beneficial than TACE in certain clinical settings. The choice of RE versus TACE still largely remains one of operator, patient, and referring provider's preference, and there are clear institutional biases for one treatment over the other. It is the authors' opinion that both procedures should be offered by interventional radiology departments, to allow the greatest latitude in the treatment of patients with liver-dominant malignancies.

Until one becomes facile with RE as a procedure, it can seem more technically challenging to perform compared with TACE. The technical administration of the agent is not the difficult part of the procedure; interventional radiologists (IRs) are experts at placing catheters where they need to be, and administering embolic agents of all sorts into arteries supplying any organ in the body. The difficulties with RE arise more from the technical specifics due to administering highly radioactive particles themselves, and occur due to the great need to protect both the patient and the operating staff from unintentional administration of radioactivity. The particular steps in the process that distinguish RE from TACE include dosimetry calculations, embolization of extrahepatic collaterals, and the inability to freely move a catheter through which radioactive particles have already been injected. It is the latter issue that is the topic of this article.

Technical Options for Hepatic Arterial Flow

Standard hepatic arterial anatomy (proper hepatic artery bifurcating into single right and left hepatic arteries) are

observed in fewer than 50% of patients. Anomalous origins of the undivided right and left hepatic arteries, most typically from the superior mesenteric and left gastric arteries, respectively, generally pose no specific technical difficulties for RE (unless whole liver therapy is anticipated). The next most common anomaly noted, and the one that causes the most difficult when planning for RE, is a distinct origin of the segment 4 hepatic artery, often termed a middle hepatic artery (►Fig. 1). The most common variant associated with this anomaly is the absence of an undivided left hepatic artery; rather, two distinct arterial origins for the normal left hepatic artery distribution (segment 2/3, and segment 4) are noted. If left lobe RE is planned, this anomaly provides a challenge for the IR that is specific for RE procedures.

Unlike TACE (or most other embolizations), once radioactive particle administration has begun it is generally considered a contraindication to move the catheter from its initial position. This is due to two reasons: first, if any radioactive particles remain in the catheter, there is the possibility of dislodging them into a nontarget vascular distribution upon moving the catheter. Second, there is significant risk to the operator of unwanted radiation exposure to their hands if any radioactive particles remain in the catheter. For these reasons, patients with multiple arteries supplying the intended target distribution present a challenge to the operator; significant planning must occur before the day of yttrium-90 (Y90) administration.

There are several options for patients with multiple arteries supplying the vascular distribution for Y90 administration. These include having two distinct administration setups on the day of RE; performing two different procedures on two different days; using flow-directed catheter repositioning during microsphere administration; having

Figure 1 Celiac angiogram demonstrating multiple hepatic artery anomalies. Open black arrow—undivided right hepatic artery. Solid black arrow—segment 4 (middle hepatic) artery. Solid white arrow—isolated segment 2/3 hepatic artery. Open white arrow—accessory segment 3 hepatic artery.

one administration setup with a flow-dividing system; doing a partial administration through a single administration setup and changing out delivery catheters; or performing embolization of one of the vessels to promote intrahepatic flow redistribution.

Two Distinct Administration Setups

The main benefit of having two distinct administration setups is the minimal likelihood of an inadvertent yttrium spill. In addition, very precise dosimetry can be performed and very exact delivery of calculated doses can be accomplished into each distribution. To perform the procedure in this way, two distinct yttrium dose vials must be used. For resin beads, this requires division of the single-ordered dose vial into two distinct vials by the nuclear medicine/radiation physicist on the day of administration; conversely, two different dose vials may be ordered, which is also the procedure required for glass beads. As the manufacturers of the two radioembolic devices presently commercially available in the United States charge for microspheres on a per administration or per treatment session basis—and not on a per vial basis—treatment of two or more separate vessels using distinct dose vials in sequential fashion during the same procedure does not add additional cost to the overall cost of the procedure. The benefit of this approach is maintenance of a conventional administration setup and preservation of radiation safety, although the requirement for serial placement and removal of separate base catheter and coaxial microcatheter systems into target vessels for individual administrations extends procedure length.

There are many options for the use of two administration setups, but all require the placement of two microcatheters into each distinct artery supplying the vascular distribution of interest. As noted previously, these catheterizations may be performed in sequential fashion during one Y90 RE therapy via a single standard 5-Fr vascular access. Alternatively, one 6- or 7-Fr guide catheter may be placed into the common hepatic

artery, and then by using a Y-adaptor place two microcatheters into each distribution via the single guide catheter.

Performing Two Procedures on Two Different Days

Perhaps the least complex method by which to deal with multiple arteries supplying the same vascular distribution is to perform multiple procedures on the same patient. Although this makes everything easier, from dosimetry to delivery, there are several drawbacks to such an approach. First, the patient must return for at least one more procedure, leading to a delay in treating the entire target distribution as well as the inconveniences of the postprocedure safety measures. Second, multiple procedures will significantly add to the costs of the procedure (angiographic materials cost, procedure fees, and the added Y90 dose vial expense). Finally, insurance preauthorization may be difficult due to the added procedure and associated costs.

Flow-Directed Catheter Repositioning

Flow-directed catheter repositioning may be used to relocate a microcatheter midway through resin microsphere administration. With this method, a microcatheter is positioned in a desired branch vessel for infusion, and then at some point during the administration, the catheter is maneuvered without a guidewire (and without violating the closed administration setup) into a second branch vessel for completion of RE. The ability to inject iodinated contrast material as a component of the resin microsphere administration system permits the flow-directed repositioning; in applying this technique, the operating IR retracts the indwelling microcatheter from the primarily selected tumor feeding vessel and advances it into a second tumor supplying branch, while simultaneously injecting contrast material for guidance as well as confirmation of final catheter position. This technique works well for vessels in which separate administration is desirable but that lie in close proximity and are easily selectable without a guidewire. An example is the anterior and posterior segmental branches of the right hepatic artery if administration distal to cystic artery is preferred. Conversely, this method is not applicable for branches arising from distinct vascular distributions in which a reselection could not easily be performed without significant catheter manipulation or use of a guidewire, such as a replaced left hepatic artery segment 2/3 branch arising from the left gastric artery and middle hepatic artery arising from the right hepatic artery.

Because the flow-directed catheter repositioning method is limited by the inability to use a guidewire for the second vessel selection, the more difficult vessel selection often determines the first catheter position for initial Y90 administration. The technical feasibility to perform a planned flow-directed maneuver can be tested at the time of mapping arteriography. Drawbacks of this method include the potential for β radiation to the IR during catheter manipulation (clearing the microcatheter of microspheres before handling

and holding the catheter with gauze is recommended) and likelihood for unpredictable dose administration to the different vessels. Moreover, this approach is not applicable for glass microspheres due to lack of iodinated contrast in the administration setup and relatively shorter delivery duration. Despite minor shortcomings, the flow-directed catheter repositioning method has the benefit of circumventing use of a second dose vial, avoiding placement of a second catheter system, and preventing need for flow dividers or breaching the closed administration system (as discussed later).

One Administration Setup with a Flow Divider

Another option is to have one administration setup and one dose vial, and to divide the Y90 particles once they leave the administration setup but before they reach the patient. This generally requires a jury-rigged delivery system that uses a Y-adapter placed onto the efferent delivery tubing (outside of the box—toward the patient), with the two downstream tubing systems each separately attached to individual

Figure 2 Flow redistribution performed due to left hepatic artery anomalies. (A) Celiac angiography demonstrating undivided right hepatic artery (open black arrow), segment 4 hepatic artery arising from the right hepatic artery (open white arrow), and separate origins of the segment 2 (solid white arrow) and segment 3 hepatic arteries (solid black arrow). The plan for this patient (who needed both right and left hepatic artery Y90 embolizations due to diffuse bilobar metastatic disease) was to treat the right hepatic and segment 4 hepatic artery distributions with one infusion, and the left hepatic artery distribution from a separate single infusion. To accomplish this single left hepatic artery infusion, it was decided to embolize the segment 2 branch and allow intrahepatic collaterals to develop from the segment 3 hepatic artery. (B) Angiography of the common hepatic artery following embolization of the gastroduodenal artery. The separate origins of the segments 2 and 3 hepatic arteries are visualized (circle). Open black arrow—right gastric artery, which also underwent protective embolization. (C) Proper hepatic angiography following embolization of the segment 2 hepatic artery demonstrating complete proximal occlusion. The most proximal coil overlays but is not in the segment 3 hepatic artery. (D) Diagnostic angiography performed on the day of Y90 administration into segment 2/3 (~2 weeks after, A–C). Segment 3 hepatic angiography demonstrates reflux into the right hepatic artery (arrowhead). Also demonstrated is reconstitution of the intrahepatic segment 2 hepatic artery (arrow). (E) Delayed phase angiogram demonstrating near-complete coverage of the occluded segment 2 hepatic arterial distribution.

delivery catheters. Advantages of this method include only needing one delivery system and one dose vial, as well as completely contained systems. Disadvantages include the difficulty with placing two catheters as discussed earlier. More importantly, the amount of dose delivered to each catheter is completely random; the percentage of the entire dose delivered to one catheter over the other may be anywhere from 0 to 100%. Dosimetry and dose delivery are therefore largely guesswork, and the risk of over- or under-treating one distribution is largely left to chance.

Partial Administration through One Catheter, Then Changing Catheter Systems for Second Infusion Using the Same Dose Vial and Delivery Setup

With this method, the catheter is placed in one of the vessels and a partial dose is delivered via this catheter. The incomplete dose is then flushed multiple times with saline to ensure the catheter and delivery system are clear of Y90 particles; the efferent tubing coming from the delivery box is capped in sterile fashion, and the delivery catheter is removed using standard technique. A second catheter (and base catheter, as necessary) is then placed in the second vessel to undergo RE. The advantage of this method is that one dose vial and one setup are used; the main two drawbacks to this method are that the amount of dose delivered to each distribution is again nearly entirely random, and the likelihood of a radioactive spill is relatively high because the normally closed system is compromised. In fact, one author (C.E.R.) has only had spills when using this method—and over half of the time this method was used, it was complicated by a spill! Finally, this method may be particularly difficult to perform with the glass bead delivery system because most of the beads are delivered with the first saline flush; in addition, the bead vial cannot be visualized during the delivery and estimating how many beads are delivered in the first vessel is nearly impossible. With these substantial shortcomings and risks, the authors have largely abandoned this approach and suggest that it may be prudent to use one of the other described approaches to avert radioactive microsphere spill or contamination.

Performing Embolization of One of the Vessels to Promote Intrahepatic Flow Redistribution

This procedure, termed “flow redistribution” by some authors, is typically performed during the pulmonary shunt/embolization procedure, as this allows significant time for collateral vessels to develop before the actual Y90 adminis-

tration procedure(s). After proximally embolizing one of the anomalous vessels (typically with coils), intrahepatic collateral vessels typically develop to supply the embolized vascular distribution (→Fig. 2). The benefit of this strategy is to significantly simplify the delivery day itself, as there is no need for multiple catheter placements or alterations to the delivery system, nor is there any increased risk of a radioactive spill. The major drawback is the assumption that the collateral vessels will develop predictably from one of the other hepatic arteries, as this has significant implications for both dosimetry and the delivery itself. For example, if the middle hepatic (segment 4) artery is embolized, collateral vessels may develop from either the right hepatic artery or from the segment 2/3 artery (or possibly from extrahepatic vessels). This makes predictable administration of the Y90 particles difficult at best.

There is no single best method by which to deal with multiple vessels supplying a single vascular distribution before Y90 administration. In some patients, anatomic considerations may make even the above techniques too unpredictable to perform, and other options such as TACE should be reconsidered, even for treatment of one tumor feeding vessel with utilization of RE for another. In many instances, this combined RE/TACE approach may be the safest and most beneficial for patients with very difficult anatomy. Each individual patient presents their own specific set of difficulties and opportunities, and tailoring the treatment for each patient is essential. Familiarity with each of the above strategies is helpful in allowing the operator to maximize the potential for complete hepatic arterial distribution coverage and treatment of the entire area of interest.

Suggested Readings

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