Technical Dos and Don'ts of Radiation Segmentectomy and Same-Day Y-90 Treatment

Contemporary radioembolization techniques and the approaches to avoid.

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Over the past 15 years, yttrium-90 (Y-90) radioembolization has emerged as an effective locoregional treatment for hepatocellular carcinoma (HCC) and hepatic metastases.[1,2] The PREMIERE trial demonstrated a significantly longer time to progression in HCC patients treated with radioembolization when compared to conventional transarterial chemoembolization (> 26 vs 6.8 months, respectively).[3] As technologies evolve, it is important to optimize clinical efficacy, cost, and patient comfort/convenience. Radiation segmentectomy is one such advancement and is now considered an ablative tool that is potentially curative. Same-day radioembolization is a concept that serves to minimize the number of procedures, reduce cost, and maximize patient convenience. This article discusses the dos and don'ts of radiation segmentectomy and same-day Y-90.

RADIATION SEGMENTECTOMY

Radiation segmentectomy involves superselective administration of a high (ablative) dose (≥ 190 Gy) of radiation to the segmental or subsegmental arterial branch feeding the tumor-bearing segment.[4] Studies have shown that the clinical efficacy of radiation segmentectomy can be considered potentially curative.[5]

Dos of Radiation Segmentectomy

- **Do select appropriate patients and understand the goal of therapy (eg, definitive, bridge to resection, bridge/downstage to liver transplantation, curative, palliative).**
  - Solitary HCC: Solitary HCC with tumor size < 8 cm and/or sparing one or two adjacent segments may be amenable to radiation segmentectomy.[6,7]
  - Unilobar multifocal HCC (modified radiation lobectomy): Patients with multifocal unilobar tumors can undergo radiation segmentectomy to the index (largest) lesion while lobar or subselective Y-90 can be administered to the rest of the tumors.[8,9] This may allow the patient to become a resection candidate with treatment of unilobar disease and hypertrophy of the contralateral lobe. Multiple treatment sessions may be needed to achieve this effect.
  - Bilobar multifocal HCC: Treatment of bilobar multifocal HCC is difficult. Radiation segmentectomy may still have a role, and definitive treatment may have to be split into multiple treatment sessions.
  - Metastatic disease: Selective treatment can be considered for hypervascular metastatic disease (metastatic neuroendocrine tumors, cholangiocarcinoma). Given the nature of metastatic colorectal cancer (hypovascular and presence of micrometastatic disease), lobar infusions may be necessary. Liver dysfunction in the setting of hepatic metastatic disease is associated with poor survival and in most cases excludes patients from locoregional therapeutic options. The concept of radiation segmentectomy needs to be further studied in the setting of metastatic disease.
  - Hyperbilirubinemic patients: Because superselective radiation segmentectomy spares the normal non–tumor-bearing parenchyma,[10,11] it can be performed in hyperbilirubinemic patients whose bilirubin has remained relatively stable in the month(s) leading to treatment. This selective treatment can allow patients to be bridged or downstaged to liver transplantation.

- **Do meticulous mapping to confirm that the tumor is being supplied by the vessels that supply the tumor-bearing segment(s), and do cone-beam CT to confirm enhancement of all the tumor(s) within the segment(s). Consider interrogating alternate supply if this is not the case.**
  - Planning angiography should identify an angiographically isolatable tumor with two or fewer hepatic segments being perfused at the intended catheter position.
  - Prophylactic coil embolization is rarely performed in patients undergoing radiation segmentectomy using Y-90 glass microspheres, given their low rate of reflux in addition to the selectivity of the method of administration.[12]
  - A cone-beam CT run during planning angiography is essential to provide a three-dimensional (3D) delineation of the perfused liver tissue bearing the tumor.[13]
  - Macroaggregated albumin (MAA) administration for lung shunt fraction (LSF) estimation is preferably done by lobar injection, either within the right hepatic artery or left hepatic artery,[14] to minimize catheterization of the segmental artery.

- **Do plan treatment after understanding the vascular anatomy and degree of subselection.**
  - Y-90 vials are administered either in the artery supplying the two tumor-bearing segments (eg, anterior right hepatic for tumors located at segments 5/8 or posterior right hepatic artery for segment 6/7 tumors) or the segmental arterial branch feeding the tumor-bearing segment.[4] Sometimes further selection of a subsegmental branch clearly supplying the tumor is also possible.
  - Radiation segmentectomy implies applying a target dose of > 190 Gy to the HCC-bearing segment (doses > 190 Gy were associated with higher rates of complete pathologic necrosis).[15] Administered doses to the tumor-bearing segment can be as high as 500 to 1,000 Gy depending on the volume of the injected segment(s).
  - Comparing pretreatment cone-beam CT to posttreatment cross-sectional imaging can help identify incomplete tumor targeting.[13]

- **Do recognize that multiple vessel catheterizations may be necessary to perform radiation segmentectomy for segment I (caudate) tumors.**[16]

Don'ts of Radiation Segmentectomy

- **Don't give very high doses to tumors around the porta hepatis.** Segment IVb radiation segmentectomy may incur risk of biliary injury.

- **Don't forget to interrogate extrahepatic parasitized vasculature, such as internal mammary arteries or inferior phrenic arteries, if dome tumor(s) do not respond on the follow-up imaging.**

SAME-DAY RADIOEMBOLIZATION

Same-day Y-90 is where planning angiography, technetium-99m MAA scanning, and Y-90 treatment are performed in a single-day session.[17,18] Same-day Y-90 can be performed in patients with solitary or multifocal disease. However, patients who are candidates for radiation segmentectomy are the best candidates for same-day Y-90, provided that MAA results are consistent with the pretreatment estimates of LSF. Advantages of same-day Y-90 include convenience for the patient and the care team. Additional reasons to consider this approach include:

- Selected patients who initially present with borderline T2/T3 tumors would benefit from immediate treatment in order to be listed for transplant or maintain their status on the transplant waiting list[18]
- The hepatic artery is difficult to access (eg, abdominal aortic dissection requiring complex access)
- General anesthesia is required for the procedure because the patient is unable to tolerate moderate sedation
- The patient lives a long distance and cannot come twice for treatment (eg, international patients)

Dos of Same-Day Y-90

- **Do meticulous pretreatment imaging review and clinical workup.** Reviewing recent high-quality cross-sectional abdominal imaging (multiphasic CT or preferably MRI) is essential. After identifying the best treatment approach for the detected tumor(s) (typically solitary tumors are the best candidates for same-day Y-90), 3D images of the tumor-bearing parenchyma are reconstructed from the delayed venous phase. These images are used to estimate the hepatic volume that will be receiving treatment.

- **Do perform dosimetry, keeping various treatment options in mind.** Target dose is estimated by the nuclear physicist using volumetric data obtained from the 3D reconstruction of baseline cross-sectional imaging. As a precaution, all HCC patients are considered to have an LSF of 10%, while liver

metastases would have an LSF of 5%. Based on those estimates, a provisional lung dose can be calculated, and accordingly, multiple Y-90 vials can be ordered for the specific treatment day with the desired dose. Ordering multiple vials ensures: (1) on-site adjustment of doses in the event of any surprisingly elevated LSF values, (2) an effective strategy in treating watershed tumors for which a single vial will result in incomplete treatment (residual tumor), and (3) possible treatment of multiple vessels (in cases of tumors having supply from different arteries).

- **Do plan the details of the treatment day.**
  - Patients are prepped only once, and the femoral sheath remains in place until the end of the treatment session.
  - Planning angiography is performed and tumor-perfusing blood vessels are identified, followed by a cone-beam CT that confirms the volume of perfused liver parenchyma and tumor. Coil embolization of any aberrant blood supply can be performed in this session as well. Only 5% of patients who undergo same-day Y-90 also receive coil embolization in the setting of glass microspheres.[12,18]
  - Once target vessels have been identified, a small dosage of 2 mCi of MAA is administered and then the patient is transferred to nuclear medicine for LSF assessment. It is important to note that patients who receive same-day Y-90 only undergo planar scintigraphy. Single-photon emission CT is not performed for these patients given its lengthy duration.
  - Accompany the patient to nuclear medicine and make sure access site sterility is maintained and the sheath is minimally manipulated during transportation. The nurse, technologist, and physician should accompany the patient to nuclear medicine for monitoring.
  - Ensure proper coordination between the interventional radiology and nuclear medicine departments, which allows both accurate dosimetry planning as well as quick patient transport between both departments on the treatment day. Therefore, minimal time is lost in the transition phases between the three sessions of same-day treatment (eg, planning angiography, nuclear scan, and Y-90 treatment).
  - Once planar scintigraphy determines the actual LSF, just-in-time dosimetry adjustments are done. The patient is then transported back to interventional radiology to undergo the planned Y-90 treatment. By the time the patient returns to the angiography suite, the LSF should have been determined and final dosimetry adjustments made.
  - Patients are maintained on continuous conscious sedation throughout the entire same-day Y-90 session. Sedation is stopped only after treatment is complete. The entire duration of the same-day Y-90 treatment takes an average of 2.5 hours from the time the patient enters the interventional radiology room for angiography until he/she leaves the room after treatment.[18]

Don'ts for Same-Day Y-90

- **Don't select the wrong patients for this approach.** Patients with complex history or advanced disease are not ideal candidates for same-day Y-90 treatment.[7] Examples of these patients include:
  - Patients with malignant vascular invasion, especially hepatic vein thrombosis, because they usually have high LSF
  - Patients with infiltrative tumors or tumor burden > 50% of entire hepatic volume, which has been associated with high LSF
  - Patients with a poor glomerular filtration rate not on dialysis, as there is a risk of using a lot of contrast for the diagnostic and treatment angiograms

- **Don't maintain access to the hepatic artery when the patient is being transferred to nuclear medicine (unless it is a very difficult hepatic arterial access, which will require a second pressure bag).** It is preferable to leave an angled 5-F catheter in the abdominal aorta.

CONCLUSION

Radiation segmentectomy has demonstrated high safety and efficacy in treating liver malignancies. This approach may be considered "curative" in a select group of HCC patients. Proper patient selection and a thorough understanding of both segmental/subsegmental vasculature and ablative doses lead to successful treatment. Same-day Y-90 is convenient for patients and can save both costs and time (an average 2.5-hour door-to-door time). Careful patient selection and coordination with nuclear medicine are key to implementing same-day Y-90. ■

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