Radioembolization with Yttrium-90 in Patients with Unresectable Hepatocellular Carcinoma and a Transjugular Intrahepatic Portosystemic Shunt: A Case Report

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Introduction

According to the SEER Registry, it is estimated that liver cancer will account for 2.4% of all new cancer diagnoses and 5.0% of all cancer deaths in 2018. This translates to 42,220 new cases and 30,200 deaths (1). Among the various histological presentations, hepatocellular carcinoma (HCC) is the most common primary liver cancer in both men and women worldwide (2). A majority of patients present with advanced disease (3), often resulting in the concomitant presentation of liver cirrhosis and portal hypertension. Consequently, these patients have historically been ineligible for resection or transplantation and had few treatment options available until recently.

Locoregional therapy for unrespectable HCC such as transarterial chemoembolization (TACE) has been shown to be efficacious in both a remedial role, and as a bridge to transplantation (4). However, a newer brachytherapy-based alternative to TACE known as transarterial radioembolization (TARE) has been developed. TARE uses yttrium-90 (Y-90) infused glass microspheres to deliver high energy β-radiation to HCC lesions (Figure A), and has demonstrated significantly better overall survival, time-to-progression, less complications such as abdominal pain (5), and less toxicity (6) as opposed to TACE.

Both TACE and TARE rely on dual blood supply of the liver, i.e. systemic oxygenated blood flow from the hepatic arteries and venous blood from the GI tract via the portal vein. Thus, targeted arterial embolization via TACE or TARE not only mitigates the risk of an ischemic event within the liver, but also offers high dose therapy while sparing surrounding normal parenchyma. However, one major challenge to the use of transarterial therapies are patients with transjugular intrahepatic portosystemic shunts (TIPS). A TIPS diverts portal venous blood directly into the inferior vena cava thus bypassing the liver in an effort to relieve portal hypertension causing esophageal varices and refractory ascites. This does, however, come at the detriment of rendering the liver solely dependent on hepatic artery perfusion alone, and thus vulnerable to ischemic necrosis if blood flow is impaired. As a result, the use of TIPS in combination with intraarterial embolization therapy has been considered by some to be a relative contraindication in patients with HCC and portal hypertension (7,8).

However, recent studies have shown that TACE is a safe and effective therapy for patients with TIPS and adequate liver function (9-12). The use of Y-90 in the setting of TIPS has not been as well studied, although recent work by Donahue *et.al.* (13) and Padia *et.al.* (6) does suggest such an approach can be both safe and efficacious. **In that spirit, we report the case of a 68-year-old female patient with unresectable HCC (21.03 x 23.12 mm) and TIPS in the setting of chronic Hep. C and cirrhosis treated with Y-90 and the subsequent remarkable outcome.**

Methods

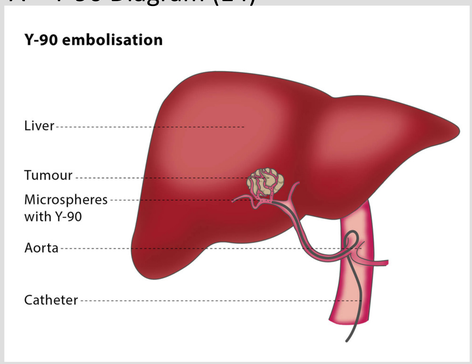
- Post MRI and serum lab screening, and despite a stable but high baseline bilirubin (2.4 mg/dl), the patient underwent a pre-Y-90 treatment hepatic arteriographic workup-up in order to map vascular anatomy, evaluate arterial blood flow, coil embolize an aberrant vessels within the vicinity of the lesion exhibiting back flow, and estimate the percentage of Y-90 shunted to the lungs via an 4mCi embolus of Tc-99 labeled macroaggregated albumin (Figure B).
- Twelve days post work-up, SirSphere Y-90 treatment was performed via the distal aspect of the right hepatic artery followed by a confirmatory Bremsstrahlung scan.
- Subsequent abdominal MRIs were performed in order to evaluate hepatic function, tumor burden, and treatment response.

Results

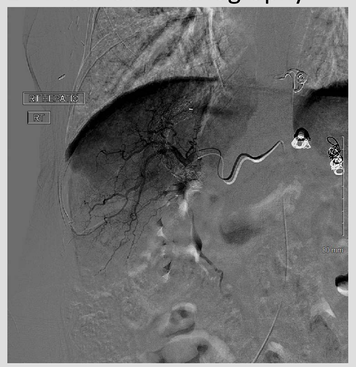
- MRI revealed a hypervascular lesion within the right hepatic lobe involving segments 5 and 6 and measuring 21.03 x 23.12 mm. Labwork indicated an α-fetoprotein (AFP) level of 13,441.
- Pre-Y-90 arteriography indicated unidirectional arterial blood flow in the vicinity of the lesions, and thus coil-embolization of any accessory arteries was not necessary.
- Lung shunt was measured at 8% (well below the 20% threshold).
- Y-90 treatment successfully delivered 0.8GBq to the right hepatic lobe.
- Bremsstrahlung activity was measured 2.5 hr. post treatment. No extrahepatic shunting, gallbladder or spleen uptake was evident. No evidence of significant post-therapeutic complications.
- Post treatment MRIs (Figures C-F) show a **progressive decrease in tumor burden: from 21.03 x 23.12 mm to 6 x 8 mm**.
- **AFP decreased from 13,441 to 3.0** 299 days post treatment.

Figures

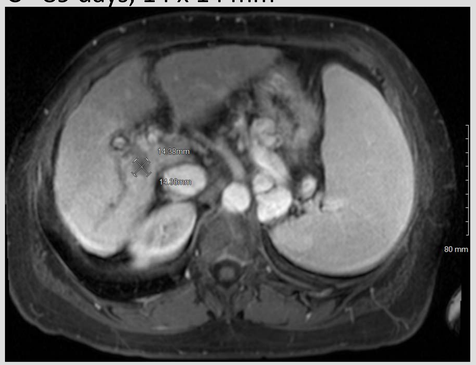
A – Y-90 Diagram (14)



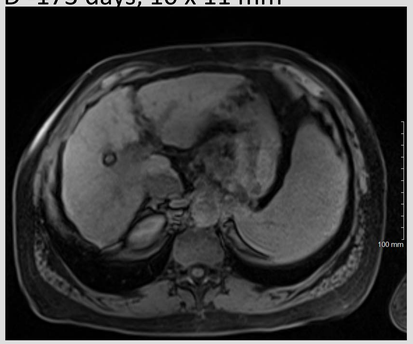
B - Pre-Y-90 Arteriography



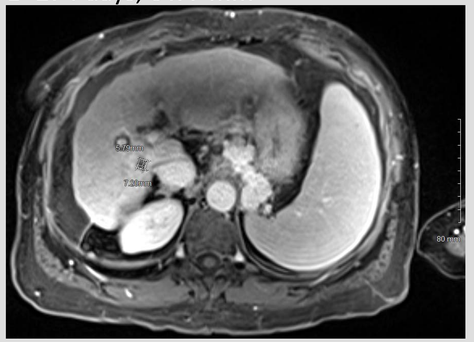
C - 89 days, 14 x 14 mm



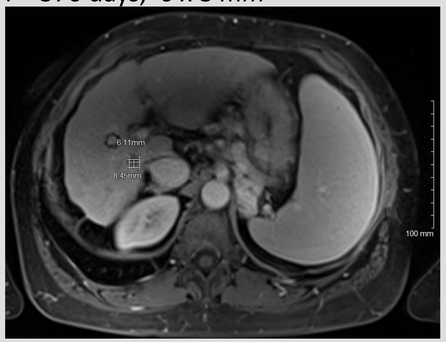
D -173 days, 10 x 11 mm



E -274 days, 6 x 7 mm



F - 376 days, 6 x 8 mm



A: Y-90 embolization schematic diagram. **B**: Digital subtraction arteriography of the right hepatic artery prior to Y-90 treatment. Patent TIPS is evident. **C-F:** MRI 89, 173, 274, and 376 days post Y-90 treatment respectively. Progressive decrease in size of the HCC lesion was observed aside from the most recent scan.

Conclusions/Future Goals

- This case report suggests Y-90 radioembolization can be both a safe and efficacious treatment for patients with unresectable HCC and TIPS. However, complete eradication of the HCC lesions was not achieved as was initially reported. This warrants further investigation.
- Future goals involve aggregation of a sufficiently large HCC-TIPS-Y-90 patient population such that a retrospective cohort study with adequate power to perform a statistical analysis could be achieved.

References

1. SEER. SEER Stat Fact Sheet: Liver and Intrahepatic Bile Duct Cancer—2018. Available at: https://seer.cancer.gov/statfacts/html/livibd.html Accessed 9/2/18
2. North, AB, South CD (2017). Cancer Incidence in Antarctica (2008-2012). In: Bray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R and Ferlay J, editors Cancer Incidence in Five Continents, Vol. XI (electronic version). Lyon: International Agency for Research on Cancer. Available from: http://ci5.iarc.fr, Accessed 9/2/2018
3. Armengol, C., et al. (2018). "Hepatocellular carcinoma: Present and future." Med Clin (Barc) **150**(10): 390-397
4. Bouchard-Fortier, A., et al. (2011). "Transcatheter arterial chemoembolization of hepatocellular carcinoma as a bridge to liver transplantation: a retrospective study." Int J Hepatol **2011**: 974514
5. Zhang, Y., et al. (2015). "Transarterial Y90 radioembolization versus chemoembolization for patients with hepatocellular carcinoma: A meta-analysis." Biosci Trends **9**(5): 289-298
6. Padia, S. A., et al. (2015). "Outcomes of Locoregional Tumor Therapy for Patients with Hepatocellular Carcinoma and Transjugular Intrahepatic Portosystemic Shunts." Cardiovasc Intervent Radiol **38**(4): 913-921
7. Hepatotoxicity after transarterial chemoembolization and transjugular intrahepatic portosystemic shunt: do two rights make a wrong?" J Vasc Interv Radiol **24**(1): 68-73
8. Kuo, Y. C., et al. (2013). "Efficacy of TACE in TIPS patients: comparison of treatment response to chemoembolization for hepatocellular carcinoma in patients with and without a transjugular intrahepatic portosystemic shunt." Cardiovasc Intervent Radiol **36**(5): 1336-1343
9. Tesdal, I. K., et al. (2006). "Percutaneous treatment of hepatocellular carcinoma in patients with transjugular intrahepatic portosystemic shunts." Cardiovasc Intervent Radiol **29**(5): 778-784
10. Wang, Z., et al. (2014). "Repeated transcatheter arterial chemoembolization is safe for hepatocellular carcinoma in cirrhotic patients with transjugular intrahepatic portosystemic shunt." Diagn Interv Radiol **20**(6): 487-491
11. Miura, J. T., et al. (2015). "Safety and efficacy of transarterial chemoembolization in patients with transjugular intrahepatic portosystemic shunts." HPB (Oxford) **17**(8): 707-712
12. Qiu, B., et al. (2015). "Combined transjugular intrahepatic portosystemic shunt and other interventions for hepatocellular carcinoma with portal hypertension." World J Gastroenterol **21**(43): 12439-12447
13. Donahue, L. A., et al. (2013). "Yttrium-90 radioembolization for the treatment of unresectable hepatocellular carcinoma in patients with transjugular intrahepatic portosystemic shunts." J Vasc Interv Radiol **24**(1): 74-80
14. Y-90 Embolisation." *CIRSE - Innovation | Education | Intervention*, cirse.org/index.php?pid=1083.

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