CLINICAL STUDY

# Outcomes of Radioembolization in the Treatment of Hepatocellular Carcinoma with Portal Vein Invasion: Resin versus Glass Microspheres

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## ABSTRACT

**Purpose:** To compare outcomes of yttrium-90 radioembolization performed with resin-based ($^{90}$Y-resin) and glass-based ($^{90}$Y-glass) microspheres in the treatment of hepatocellular carcinoma (HCC) with associated portal vein invasion.

**Materials and Methods:** A single-center retrospective review (January 2005–September 2014) identified 90 patients ($^{90}$Y-resin, 21; $^{90}$Y-glass, 69) with HCC and ipsilateral portal vein thrombosis (PVT). Patients were stratified according to age, sex, ethnicity, Child-Pugh class, Eastern Cooperative Oncology Group status, α-fetoprotein > 400 ng/mL, extent of PVT, tumor burden, and sorafenib therapy. Outcome variables included clinical and laboratory toxicities (Common Terminology Criteria Adverse Events, Version 4.03), imaging response (modified Response Evaluation Criteria in Solid Tumors), time to progression (TTP), and overall survival (OS).

**Results:** Grade 3/4 bilirubin and aspartate aminotransferase toxicities developed at a 2.8-fold (95% confidence interval [CI], 1.3–6.1) and 2.6-fold (95% CI, 1.1–6.1) greater rate in the $^{90}$Y-resin group. The disease control rate was 37.5% in the $^{90}$Y-resin group and 54.5% in the $^{90}$Y-glass group ($P = .39$). The median (95% CI) TTP was 2.8 (1.9–4.3) months in the $^{90}$Y-resin group and 5.9 (4.2–9.1) months in the $^{90}$Y-glass group ($P = .48$). Median (95% CI) survival was 3.7 (2.3–6.0) months in the $^{90}$Y-resin group and 9.4 (7.6–15.0) months in the $^{90}$Y-glass group (hazard ratio, 2.6; 95% CI, 1.5–4.3, $P < .001$). Additional multivariate predictors of improved OS included age < 65 years, Eastern Cooperative Oncology Group status < 1, α-fetoprotein ≤ 400 ng/mL, and unilobar tumor distribution.

**Conclusions:** Imaging response of $^{90}$Y treatment in patients with HCC and PVT was not significantly different between $^{90}$Y-glass and $^{90}$Y-resin groups. Lower toxicity and improved OS were observed in the $^{90}$Y-glass group.

## ABBREVIATIONS

AST = aspartate aminotransferase, BSA = body surface area, CI = confidence interval, CP = Child-Pugh, HCC = hepatocellular carcinoma, HR = hazard ratio, OS = overall survival, PVT = portal vein thrombosis, TTP = time to progression, TTT = time to toxicity, $^{90}$Y = yttrium-90

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Figures E1 and E2 and Tables E1 and E2 are available online at *www.jvir.org*.



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In hepatocellular carcinoma (HCC), portal vein invasion is a negative prognostic factor—present in up to 44% of patients with HCC at death (1)—that increases the chances of extrahepatic spread and decreases overall survival (OS) (2). Portal vein invasion is suspected when HCC is accompanied by adjacent portal vein thrombosis (PVT). This impairment of portal blood flow also jeopardizes perfusion to normal, healthy liver, potentially marginalizing the patient's ability to tolerate embolic transarterial therapies (3,4).

Yttrium-90 ($^{90}$Y) radioembolization is an established transarterial therapy that has been proven capable of inducing significant tumor necrosis and delaying disease progression (5–7). The minimally embolic nature of radioembolization has made the treatment of HCC with associated PVT an increasingly common indication for its use (8–10). At the present time, there are two intraarterial vectors for the delivery of $^{90}$Y approved by the US Food and Drug Administration: a resin-based device (SIR-Spheres; SIRTeX Medical Limited, Inc; North Sydney, Australia) and a glass-based device (TheraSphere; BTG International Ltd; London, United Kingdom). Each vector makes use of microspheres to facilitate intraarterial administration of $^{90}$Y (11). Although both forms of radioembolization have been proven capable of achieving favorable responses (12,13), differences between the glass-based and resin-based devices with regard to microsphere composition, size, degree of embolic effect, and specific activity per sphere are known to exist (11). Glass-based $^{90}$Y therapy ($^{90}$Y-glass) is considered minimally embolic but capable of delivering a specific activity of up to 2,500 Gbq/sphere, whereas resin-based $^{90}$Y therapy ($^{90}$Y-resin) has been described as moderately embolic with an activity per sphere of 50 Gbq/sphere (11). These differences combined with surmised benefit of a minimally embolic transarterial therapy in the treatment of HCC in patients with a compromised portal blood supply formed the basis for our decision to compare the outcomes of $^{90}$Y-resin and $^{90}$Y-glass in the treatment of HCC with associated PVT.

## MATERIALS AND METHODS

### Study Design

This single-center study was compliant with the Health Insurance Portability and Accountability Act and approved by the local institutional review board. Data were obtained searching the Epic electronic medical record system (Epic Systems Corporation, Verona, Wisconsin). From January 2005 to September 2014, 709 patients treated with $^{90}$Y radioembolization were reviewed. Imaging studies performed before the procedure were retrospectively reviewed by an independent, board-certified radiologist. Patients included in the study had unresectable HCC with associated main or lobar PVT on their most recent imaging study within a 90-day period before the procedure and received ipsilateral $^{90}$Y radioembolization. Extension into the main portal vein (occlusive or nonocclusive) was categorized as "main" PVT. HCC was diagnosed by the American Association for the Study of Liver Diseases guidelines in all cases (14,15). The following patients were excluded: patients who underwent prior ipsilateral $^{90}$Y therapy (n = 2), patients who received both resin-based and glass-based therapy (n = 2), and patients with PVT contralateral to the side of $^{90}$Y treatment (n = 1). Patients with extrahepatic metastasis were not excluded. The decision regarding which patients to treat with $^{90}$Y was reached by consensus at a weekly multidisciplinary conference of hepatologists, oncologists, transplant surgeons, and interventional radiologists. The choice of $^{90}$Y-resin or $^{90}$Y-glass was made by the interventional radiologist performing the treatment. All data were reported in accordance with previously established radioembolization reporting standards (16).

### Patients

The criteria for inclusion in the study were met by 90 patients. Patient demographics are summarized in **Table 1**. The mean age was 65.3 years in the $^{90}$Y-glass group and 60.0 years in the $^{90}$Y-resin group ($P = .05$). The remaining baseline patient demographics were not significantly different between the two groups. There was a greater percentage of Eastern Cooperative Oncology Group status 2 patients in the $^{90}$Y-glass group (14.5%) compared with the $^{90}$Y-resin group (4.8%). Most patients (48 [53.3%]) were Child-Pugh (CP) class A with lobar PVT. There were 32 (64.4%) patients with main PVT and 20 (22.2%) CP class B patients. **Figure E1** (available online at *www.jvir.org*) is a flow diagram of the study design.

### $^{90}$Y Treatment

All patients underwent a standardized workup before treatment comprising a clinical evaluation, laboratory and imaging assessment, and a mapping procedure with technetium-99m macroaggregated albumin, all of which have been previously described (5,11,17). Dosimetry and infusion protocols for $^{90}$Y-resin and $^{90}$Y-glass therapy were followed according to manufacturer guidelines using a body surface area (BSA) dosing model for $^{90}$Y-resin treatments (11) and using a noncompartmental Medical Internal Radiation Dose Committee method of dose calculation for $^{90}$Y-glass treatments (18). $^{90}$Y therapy was administered through selective catheterization of segmental feeding arteries when possible. Lobar injection was performed when segmental feeding vessels were not clearly identified. For treatment-naïve patients with bilobar disease, a staged approach comprising multiple treatment sessions was planned (17). A standard protocol including the use of antiemetics, pain medication, intravenous hydration, and prophylactic proton-pump inhibitors after the procedure was followed in all cases, as previously described (11).