Selective Internal Radiation Therapy: Quantifying Distal Penetration and Distribution of Resin and Glass Microspheres in a Surrogate Arterial Model

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ABSTRACT

Purpose: To experimentally investigate the effects of microsphere density and diameter on distal penetration.

Materials and Methods: A surrogate hepatic arterial system was developed to replicate the hemodynamics (pressures, flow rates, pulsatile flow characteristics) and anatomic geometry (vessel diameters) proximal and distal to the microsphere injection point. A planar tumor model, placed distal to the injection point, allowed visualization of deposited microspheres. Bland resin and glass microspheres, with physical characteristics approximating the characteristics of commercially available products, were injected into the surrogate system. Microsphere type, injection rate, systemic flow rate, and tumor model inclination were varied among tests (glass, n = 7; resin, n = 6) with replicates for 2 conditions. After injection, 254 micrographs were obtained at previously defined locations throughout the tumor model to document microsphere distributions. Average microsphere distributions and mass measurements of microspheres collected at the tumor outlet were analyzed to quantify distal penetration for each case.

Results: Across all test conditions, average penetration depths of resin microspheres were higher compared with glass microspheres (45.1 cm ± 11.8 vs 22.3 cm ± 9.9). The analysis of variance indicated that the observed difference between microsphere type (glass vs resin) was significant ($P = .005$, $df = 1,2$). The observed distance means did not differ significantly across flow rate or inclination angle.

Conclusions: Penetration depths of resin microspheres were significantly higher than penetration depths of glass microspheres in the surrogate hepatic arterial system.

ABBREVIATIONS

HA = hepatic arterial, SIRT = selective internal radiation therapy, ^{99m}Tc-MAA = technetium-99m albumin aggregated, ^{90}Y = yttrium-90

Selective internal radiation therapy (SIRT) of unresectable liver tumors is performed via intraarterial injection of yttrium-90 (^{90}Y)-infused microspheres. SIRT has proven to be effective in controlling liver tumors and improving patient outcomes as a stand-alone therapy and when used in combination with systemic chemotherapy in several disease states (1). Resin and glass microspheres are commercially available, with reported differences in physical properties, most notably density and diameter. The density of glass microspheres is approximately twice that of resin (3.4 g/cm^3 glass vs 1.6 g/cm^3 resin), whereas corresponding diameter is approximately 15% smaller (25.0 μm glass vs 29.1 μm resin).

The efficacy of SIRT depends on the distal penetration and distribution of injected microspheres because insufficient coverage allows for continued tumor growth. Although multiple studies have investigated various aspects of resin and glass microsphere deposition in

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Figures E1 through E4 and Table E1 are available online at *www.jvir.org*.

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SIRT procedures (1), no study has directly compared the distal penetration of resin and glass microspheres. The deposition and tumor uptake of resin and glass microspheres have been individually compared with technetium-99m albumin aggregated (^{99m}Tc-MAA) microspheres, often used in SIRT planning as a surrogate for ^{90}Y microspheres. Published studies showed significant differences in the distributions of ^{99m}Tc-MAA and ^{90}Y microspheres when injected into identical anatomy before and after treatment. Kokabi et al (2) found significantly greater tumor uptake for ^{99m}Tc-MAA doses than for glass ^{90}Y microspheres (1.4:1). Among other factors, particle size, density, and morphology have been identified as key factors in these differences (3,4).

MATERIALS AND METHODS

A surrogate hepatic arterial (HA) system was developed to investigate experimentally the effects of microsphere density and diameter on distal penetration. Central to the design of this model was replicating the hemodynamics (pressures, flow rates, pulsatile flow characteristics) and anatomic geometry (vessel diameters) proximal and distal to the microsphere injection point. Clinically, microspheres are infused from a delivery catheter at an HA branch, usually several millimeters in diameter, where they proceed to smaller arterial branches, ideally implanting in the microvasculature of a tumor. Flow rates, vessel diameters, and pressures vary substantially from the injection point to the target location. To replicate these effects accurately, a surrogate model of human hepatic anatomy (**Fig 1**) was constructed based on three-dimensional computed tomography imaging and anatomic measurements of vessel diameters. This rigid planar model, fabricated using stereolithography processes, included left and right hepatic, gastroduodenal, and splenic arteries with flow terminating in 16 distal vessels (1.0 mm inside diameter, 2.0 mm outside diameter clear polyvinyl chloride tubing). The transparent construction allowed for direct visualization and image-based measurements of microsphere distributions. A pressure sensor was placed in the gastroduodenal artery for systemic pressure measurements, and pinch valves (numbered 1 through 16 in **Fig 1**) were included to regulate local pressures and flow rates.

Liver Tumor Model

A greater challenge was experimentally replicating the hemodynamics of liver tumors because the microvascular bed in which the microspheres embed is characterized by large numbers of branching arterioles with inner diameters of 20 μm. These characteristics make fabrication of an exact anatomic duplicate extremely difficult, if not impossible, with conventional processes. The entrapment of microspheres within such model structures would eliminate the possibility of reuse. As an alternative to replicating three-dimensional tumor anatomy, a planar tumor model (**Figs 2a, b, E1** [available online at *www.jvir.org*]), consisting of silicone microchannels sandwiched between two glass plates, was designed to achieve the functional specifications (appropriate fluid pressures, flow rates, and dimensional scale; microsphere visualization and quantification; reusability).

Published data from animal studies reveal arteriole diameters ranging from 18.0 to 24.0 μm and arteriole fluid velocities ranging from 0.4 to 6.8 mm/s (**Table E1** [available online at *www.jvir.org*]) (5–10). To match these physical characteristics, the tumor inlet fanned out from

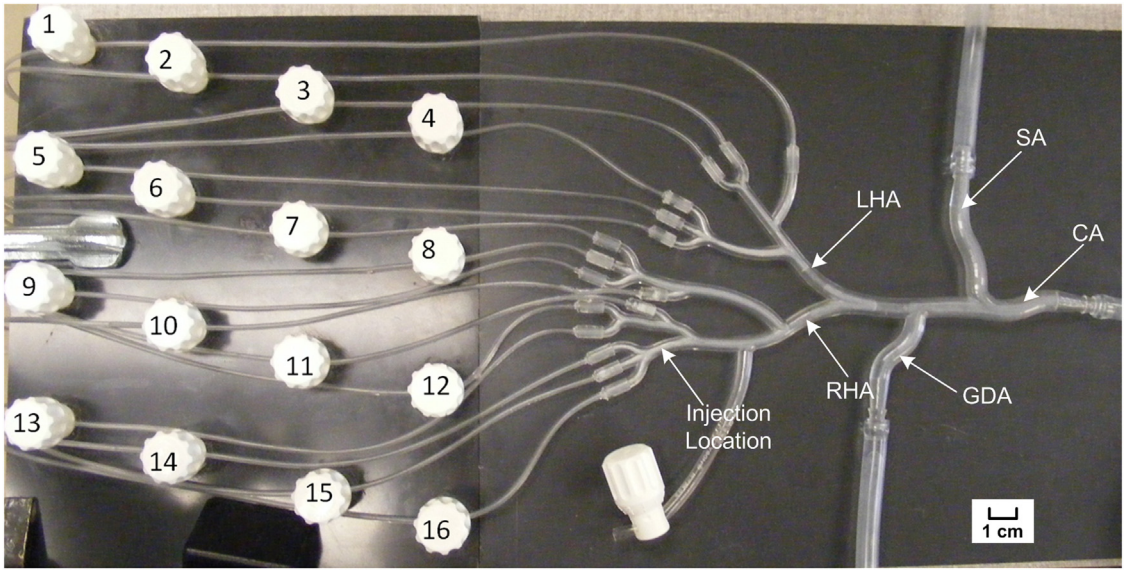

Figure 1. HA model. 1–16 = pinch valves. CA = celiac axis, GDA = gastroduodenal artery, LHA = left hepatic artery, RHA = right hepatic artery, SA = splenic artery.