A Simple Method for Estimating Dose Delivered to Hepatocellular Carcinoma after Yttrium-90 Glass-Based Radioembolization Therapy: Preliminary Results of a Proof of Concept Study

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ABSTRACT

Purpose: To investigate a simple semiquantitative method to estimate yttrium-90 (^{90}Y) dose delivered with radioembolization to infiltrative hepatocellular carcinoma (HCC).

Materials and Methods: In a prospective study, patients with infiltrative HCC and portal vein thrombosis (PVT) underwent glass-based ^{90}Y radioembolization including technetium-99m macroaggregated albumin (^{99m}Tc-MAA) hepatopulmonary shunt study before therapy and bremsstrahlung single photon emission computed tomography (SPECT)/computed tomography (CT) after ^{90}Y radioembolization. Baseline magnetic resonance imaging was coregistered with ^{99m}Tc-MAA and bremsstrahlung SPECT/CT imaging separately. Unit tumor activity (^{90}Y radioactivity delivered to each cubic centimeter of tumor) was estimated based on a lobar infusion approach. Correlation between proportions of ^{99m}Tc-MAA and ^{90}Y delivered to the tumor was investigated. Survival analysis was performed using Kaplan-Meier estimations.

Results: ^{90}Y therapy was administered in 18 consecutive patients (median age, 55.3 y; mean tumor volume, 588 cm^3). Higher intratumoral ^{90}Y dose predicted prolonged survival, with 13.2-month median survival in patients with HCC and mean ^{90}Y dose of $\geq$ 100 Gy versus 4.6-month median survival for other patients ($P < .001$). Of administered ^{90}Y dose, 51.9% was delivered to the targeted tumors compared with 74.1% of ^{99m}Tc-MAA with linear correlation between biodistribution of ^{99m}Tc-MAA and ^{90}Y observed (Pearson $r = 0.774$, $P < .001$).

Conclusions: The findings in this study suggest that approximately 50% of administered ^{90}Y dose is taken up by targeted infiltrative HCC with PVT. Intratumoral ^{90}Y dose $\geq$ 100 Gy in unresectable infiltrative HCC via a lobar intraarterial approach is a positive prognostic factor for survival.

ABBREVIATIONS

BCLC = Barcelona Clinic Liver Cancer, HCC = hepatocellular carcinoma, LSF = lung shunt fraction, PVT = portal vein thrombosis, ROI = region of interest, SPECT = single photon emission computed tomography, ^{99m}Tc-MAA = technetium-99m macroaggregated albumin, TD = tumor dose, ^{90}Y = yttrium-90

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death in the United States and around the world (1). Infiltrative HCC is an uncommon form, accounting for 7%–15% of HCC with a median overall survival of approximately 5 months (2–4). In a prospective comparative study, Lopez et al (5) showed no survival benefit from transarterial chemoembolization in patients with infiltrative HCC. Almost all patients with infiltrative HCC present with portal vein thrombosis (PVT) at the time of presentation (Barcelona Clinic Liver Cancer [BCLC] stage C) and are unsuitable candidates for surgical resection. Patients with BCLC stage C tumors were found to have a

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median survival of 4.8 months when receiving best available supportive care (6). Sorafenib, currently used as a standard of care in patients with BCLC stage C tumors, has been shown to prolong survival by 3 months (7).

In recent years, positive outcomes have been reported with the use of selective intraarterial radioembolization with yttrium-90 (^{90}Y) microspheres for treatment of unresectable HCC (8–12). Although ^{90}Y therapy is currently used as a locoregional therapy for noninfiltrative unresectable HCC, preliminary results from a prospective safety and feasibility clinical trial at this institution demonstrate that glass-based ^{90}Y is a safe and viable option for treatment of infiltrative HCC with PVT (13).

To date, very few studies have investigated the actual dose of radioactive therapy delivered to HCC and, more importantly, its implications on survival. Preliminary results from a few studies have suggested that higher ^{90}Y tumor dose (TD) predicts objective imaging response according to European Association of Study of Liver criteria assessing the degree tumor necrosis (10,14,15). However, the observed threshold ^{90}Y TD varies widely among these studies, ranging from 205–500 Gy. In a more recent study, Garin et al (12) reported that higher dose would significantly prolong survival with higher objective tumor response. In the present study, a simple semiquantitative method to estimate the biodistribution of ^{90}Y delivered to the targeted liver lobe and tumor was investigated, and correlation of intratumoral dose to overall survival in patients with infiltrative HCC with PVT was analyzed.

MATERIALS AND METHODS

Patients with advanced (BCLC stage C) infiltrative HCC and PVT (based on dynamic multiphase contrast-enhanced magnetic resonance [MR] imaging) were enrolled for glass-based ^{90}Y radioembolization therapy in a prospective, single-center safety/feasibility trial. The trial was approved by the institutional review board and was compliant with the Health Insurance Portability and Accountability Act. All patients were evaluated by a multidisciplinary team of physicians to determine the best treatment option for each individual. Patients $\geq$ 18 years with Eastern Cooperative Oncology Group performance score $\leq$ 2 and expected life expectancy of $\geq$ 3 months were screened. All patients underwent baseline dynamic multiphase abdominal MR imaging. Infiltrative HCC was defined as a geographic region with high T2 signal, arterial enhancement, and early washout on T1 gadolinium-enhanced images (2). Figure 1 illustrates an infiltrative HCC with right PVT and enhancement of tumor thrombus in the arterial phase.

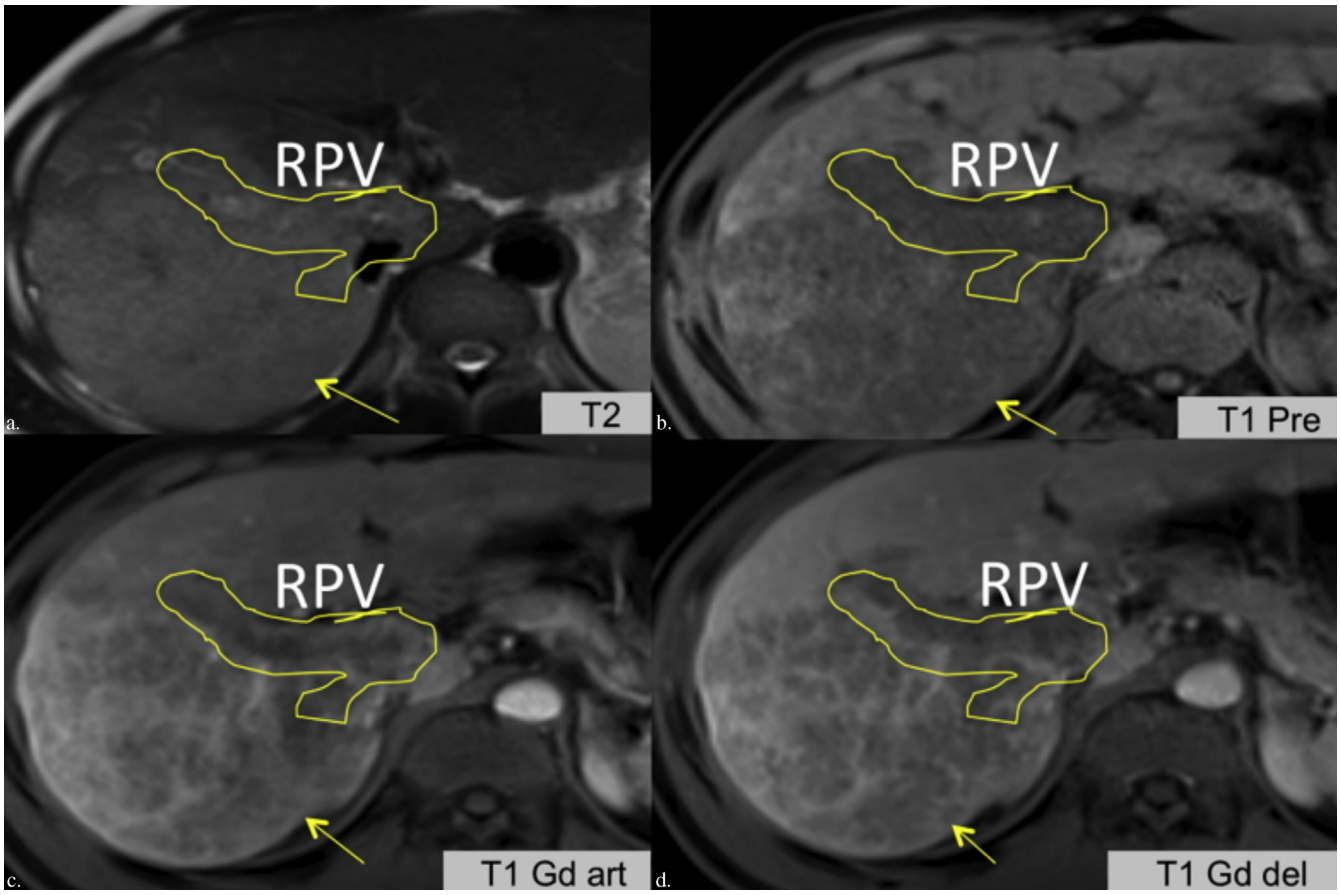

Figure 1. Infiltrative HCC with geographic arterial phase enhancement and early washout **(a–d)** and portal vein enhancement compatible with PVT.