# Reduction of Metastatic Load to Liver after Intraarterial Hepatic Yttrium-90 Radioembolization as Evaluated by [18F]Fluorodeoxyglucose Positron Emission Tomographic Imaging

**Ching-yee Oliver Wong, MD, PhD, Feng Qing, MD, PhD, Michael Savin, MD, Janice Campbell, MS, Vanessa L. Gates, MS, Kanchi M. Sherpa, MD, Robert J. Lewandowski, MD, Conrad Nagle, MD, and Riad Salem, MD, MBA**

**PURPOSE: To assess the response of hepatic metastases after treatment with intraarterial yttrium 90 radioembolization (ie, use of SIR-Spheres) with use of [$^{18}$F]fluorodeoxyglucose (FDG) positron emission tomography (PET).**

**MATERIALS AND METHODS: Nineteen patients with metastatic cancer to the liver from various solid tumors with progression despite polychemotherapy were included. All patients underwent baseline computed tomography, FDG PET, hepatic angiography, and intraarterial technetium 99m macroaggregated albumin scan for assessment of lung shunting fraction. Patients were treated with $^{90}$Y resin microspheres on a lobar basis and were monitored for 3 months with use of dedicated attenuation-corrected PET. For each patient, regions of interest were drawn along the liver edge to measure total liver standard uptake value (SUV) on axial images, covering the entire liver. Visual estimates were also performed and graded as +1, 0, −1, −2, or −3 for progression, no change, and mild, moderate, and dramatic improvement by posttreatment PET.**

**RESULTS: The median absorbed dose for the tumor was 76 Gy. There was a significant overall decrease in total liver SUV after treatment (baseline, 71,134 ± 38,055; after SIR-Sphere treatment, 59,941 ± 26,509; $P = .028$) for the entire group. Visual estimates placed 15 patients (79%) in response categories (−3 to −1) and four patients (21%) in nonresponse categories (0 to +1) for the liver. The percentage change of total liver SUV after treatment in the response group (−19%) was significantly greater and different in direction than that in the nonresponse group (+27%; $P = .03$). This percentage change was also correlated significantly with the respective visual estimates ($r = 0.72$; $P < .0005$) for each individual patient. Three patients had major complications related to hyperbilirubinemia (transient, $n = 1$; permanent, $n = 2$).**

**CONCLUSIONS: The results suggest that there is significant reduction of hepatic metastatic load as evaluated objectively by PET after $^{90}$Y radioembolization for the treatment of unresectable metastatic disease to the liver. $^{90}$Y radioembolization provides encouraging results by arresting progression of metastatic cancer to the liver.**

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**Abbreviations:** FDG = [$^{18}$F]fluorodeoxyglucose, MAA = macroaggregated albumin, PET = positron emission tomography, SUV = standard uptake value

DETECTION of metastatic cancer to the liver by positron emission tomography (PET) or computed tomography (CT) is usually an ominous sign for patients with colorectal cancer (1,2) or other solid cancers (3,4). $^{90}$Y resin microsphere radioembolization in which $^{90}$Y is the radioactive constituent of the radioembolization has been shown to be chemically feasible for in vivo delivery of $\beta$-radiation (5). Recently, hepatic intraarterial infusion of $^{90}$Y microspheres has been introduced for palliating unresectable hepatocellular carcinoma (6,7) and liver metastases from colorectal cancer (8,9). The $^{90}$Y resin microspheres, commercially available as SIR-Spheres (Sirtex Medical, North Ryde, Australia), are introduced via catheterization of the hepatic artery that supplies the majority of the blood to tumor. The microspheres are trapped in the tumor capillary bed, where they exert a local radiotherapeutic effect. $^{90}$Y, a pure

From the Positron Diagnostic Center and Medical Cyclotron, Department of Nuclear Medicine (C.O.W., F.Q., J.C., K.M.S., C.N.), and Division of Interventional Radiology, Department of Radiology (M.S., R.J.L., C.N.), William Beaumont Hospital, 3601 West 13 Mile Road, Royal Oak, Michigan 48073-6769; and Division of Interventional Radiology, Department of Radiology (V.L.G., R.S.), Northwestern Memorial Hospital, Chicago, Illinois. Received February 3, 2005; revision requested March 28; final revision received and accepted April 12. **Address correspondence to** C.O.W.; E-mail: owong@beaumont.edu

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$\beta$-emitter with a physical half-life of 64.2 hours, decays to stable zirconium 90. The average energy of the $\beta$-emissions from the $^{90}$Y is 0.9367 MeV, with an average penetration range of 2.5 mm in tissue (6). Previous studies (9,10) addressed the feasibility of the use of PET for assessing and quantifying metabolic response after intraarterial $^{90}$Y glass microspheres, commercially available as TheraSpheres (MDS Nordion, Ottawa, ON, Canada) with similar particle sizes. These studies suggest that traditional anatomic imaging is insensitive in monitoring response compared with metabolic imaging (9), justifying the use of a novel technique of objective and quantitative evaluation of tumor load reduction by PET after $^{90}$Y treatment (10). The percentage change in total liver standard uptake value (SUV) from all axial slices of the liver has been shown to correlate well with visual evaluations of metabolic response (10). However, resin-based $^{90}$Y microspheres have approximately 40–60 times more particles than glass $^{90}$Y microsphere per GBq of $^{90}$Y. It is unknown whether this metabolic response is caused by the embolic effect of the particle number, the local radiation effect that is imparted, or both. The objective of this prospective study was to evaluate the reduction of metastatic load after $^{90}$Y resin microsphere radioembolization of liver metastases from various solid cancers by [$^{18}$F]fluorodeoxyglucose (FDG) PET.

## MATERIALS AND METHODS

### Patient Group

Nineteen consecutive patients (13 men, six women; mean age, 64 years ± 13) with unresectable metastatic cancer to the liver from colorectal cancer ($n$ = 10), breast cancer ($n$ = 2), non–small-cell lung cancer ($n$ = 2), thyroid cancer ($n$ = 2), gastrointestinal sarcoma ($n$ = 1), gallbladder cancer ($n$ = 1), or adenocarcinoma of unknown origin ($n$ = 1) with tumor progression despite polychemotherapy who had pre- and posttreatment PET scans were included. All patients underwent baseline CT, FDG PET, hepatic angiography, and intraarterial technetium-99m macroaggregated albumin (MAA) scans for lung shunting fraction. All patients provided written informed consent to $^{90}$Y microsphere therapy and collection of data for research purposes under guidelines of the institutional review board. All patients were treated with $^{90}$Y radioembolization with resin microspheres on a lobar basis (9,10) and were monitored over a period of 3 months with use of FDG PET imaging.

Eligibility for $^{90}$Y treatment was based on the following inclusion criteria (10,11): age at least 18 years, Eastern Cooperative Oncology Group performance status no greater than 2, and confirmed diagnosis of metastatic cancer to the liver. Patients were excluded from treatment if they were pregnant, had significantly abnormal pretreatment laboratory findings (absolute granulocyte count <1,500/mL, platelet count <75,000/mL, serum creatinine level >2.0 mg/dL, or serum bilirubin level >3.0 mg/dL), any contraindications to angiography or selective visceral catheterization, significant extrahepatic disease representing an imminent life-threatening outcome, pulmonary insufficiency, active uncontrolled infection, or any other significant underlying medical or psychiatric illness. None of the patients received chemotherapy during the course of the treatment regimen.

### Embolization Procedure/$^{90}$Y Infusion

Treatment planning and administration of $^{90}$Y resin microspheres was performed generally according to previously published guidelines (7,10). Triple-phase liver CT was performed within 30 days before the embolization procedure and 5-mm images were reviewed with special attention to the volume of the liver and degree and distribution of tumor infiltration. When a patient was deemed a suitable candidate for $^{90}$Y microsphere treatment, a visceral arteriogram with intrahepatic arterial $^{99m}$Tc MAA scanning was obtained to define the arterial anatomy to evaluate the amount of pulmonary and gastrointestinal flow.

All treated patients were evaluated to confirm an acceptable risk of shunting of $^{90}$Y microspheres to the lungs (<30 Gy) (7). Lung shunting was assessed with use of intrahepatic arterial $^{99m}$Tc MAA scanning (shunt fraction = 100% × lung counts / [lung + liver + stomach counts]) (10). In patients with hepatic tumors, a portion of the arterial supply may bypass the capillary bed and drain directly into the venous system. Those microspheres that are not trapped in the liver will be shunted via the heart and deposited in the lungs. Therefore, a lung shunting measurement is essential before the treatment to obtain a unique shunting fraction for the given physiology and anatomy of the hepatic tumors. Before treatment, planar anterior $^{99m}$Tc MAA scans were obtained within 30 minutes after intrahepatic arterial injection of 150 MBq $^{99m}$Tc MAA during angiography to include the lungs, liver, and stomach. Lung activity of less than 10% was considered insignificant shunting. Otherwise, the treatment dose was adjusted to optimize the radiation dose given to each lobe of liver. This method of lobar treatment for $^{90}$Y glass microsphere radioembolization was recently used by our group (9–11) and differs from the whole-liver approach previously reported for hepatocellular carcinoma (7,12) and metastatic colorectal cancer (8). Each lobe of the liver was treated separately with a lobar injection.

A treatment plan according to a lobar treatment strategy was constructed for each patient. The amount of activity required for the target dose of $^{90}$Y microsphere was calculated (if ignoring lung shunt) according to the following formula (7):

$$\text{Activity (GBq)} = \text{tumor dose (Gy)} \times \text{tumor mass (kg)}/\{50 \times \text{activity uptake fraction to tumor}\}$$

The mass of the targeted lobe was determined with use of CT images for volume calculation, with a conversion factor of 1.03 g/cm$^3$. The appropriate activity was drawn into the delivery device. An activity ranging from 2.0 to 3.0 GBq of $^{90}$Y resin microspheres split between liver lobes was prescribed (13). With use of this technique, normal liver tissue exposure was less than 30–50 Gy, the level above which complications have been reported with external-beam radiation therapy (14). $^{90}$Y resin microspheres were injected into a percutaneous catheter inserted via the femoral artery and directed to the targeted liver lobe. The radiation dose