



Selective Internal Radiation Therapy (SIRT)

- Selective Internal Radiation Therapy (SIRT) is an FDA approved treatment for liver metastases from colorectal cancer
- Eligible patients have unresectable colorectal cancer metastases to the liver and no significant extra-hepatic metastatic disease, no longer respond to chemotherapy or refuse chemotherapy, or wish to have both chemotherapy and SIRT
- SIRT cannot be used if there is significant shunting of blood flow to the lungs, portal vein obstruction, or elevated bilirubin

Malignant lesions in the liver primarily receive their blood supply through arterial perfusion, whereas normal liver parenchyma is mostly fed through the portal vein. In addition, the micro-vascular density of liver tumors is 3-200 times greater than the surrounding liver parenchyma. These differences provide an opportunity to selectively deliver therapeutic agents to liver tumors, while sparing the rest of the organ. In selective internal radiation therapy (SIRT) (Figure 1), ⁹⁰Yttrium labeled resin microspheres (SIR-Spheres®) are infused into the hepatic artery and they lodge primarily in the tumor microvasculature. The treatment combines arterial micro-embolization with high-dose interstitial radiotherapy. ⁹⁰Yttrium is a beta emitter with a half-life of 64.1 hours with an average energy of 0.94 MeV. This corresponds to a maximum range of 1.1 cm within tissue with a mean path of 2.5 mm. In 2002, the FDA gave pre-market approval of SIR-Spheres® as a brachytherapy device for the treatment of metastases from colorectal cancer. SIRT has been performed at MGH over the past two years.

At this time, colorectal cancer is the cause of death in 52,000 patients annually. In most of these patients, metastatic disease is confined to the liver even at the time of death. Therefore, localized therapies are an attractive option and surgery to remove hepatic metastases due to colorectal cancer can result in long-term survival. However, the large majority of patients are not candidates for surgery, most commonly because of multiple metastases. Other alternatives include radiofrequency ablation, which is suitable if there are 3 or fewer tumors that are smaller than 3 cm each (see [Radiology Rounds, September 2004](#)), or chemotherapy, which has limited utility.



Figure 1. The SIRT delivery kit, which is designed to shield radiation and provide a closed circuit to prevent accidental spills.

Data on the outcome following SIRT are limited. In one study of 208 patients, 87% of whom had undergone first, second, and third line chemotherapy, the response rate was 85% as measured by FDG-PET scanning. The median survival for responders was 10.5 months, compared to 4.5 months for non-responding patients. In another study, in which 100 patients with extensive colorectal metastases not amenable to resection or ablation were treated in one institution, the estimated survival at 18 and 30 months was 32% ± 4.7 and 9% ± 2.9%. The majority of patients who died did so with progressive extra-hepatic disease.

Patient Selection and Preparation

Patients with colorectal metastases should be evaluated by a medical oncologist who will discuss their treatment options. SIRT is considered to be a third line option for patients with colorectal metastatic disease that is confined to the liver or with minimal extra-hepatic involvement. In most cases, they have exhausted other treatment options and no longer respond to chemotherapy, cannot tolerate or refuse chemotherapy, or choose to receive both SIRT and chemotherapy.

Patients who are considering SIRT must be evaluated prior to treatment to confirm that metastatic disease is largely confined to the liver as well as to minimize the likelihood of life threatening complications. Patients must have adequate liver functions (bilirubin <2 mg/dl), good performance status Eastern Cooperative Oncology Group status <2, portal vein patency, and adequate renal function (eGFR >30 ml/min/m²). Patients who meet these criteria and wish to consider SIRT will meet with an interventional radiologist prior to treatment to discuss the procedure and for further radiological evaluation (Figure 2).

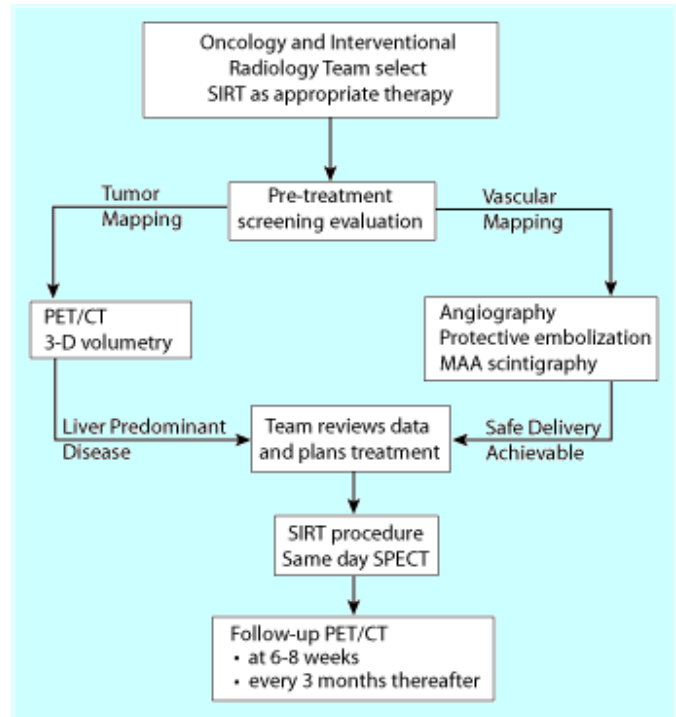


Figure 2. SIRT Therapy Flow Chart.

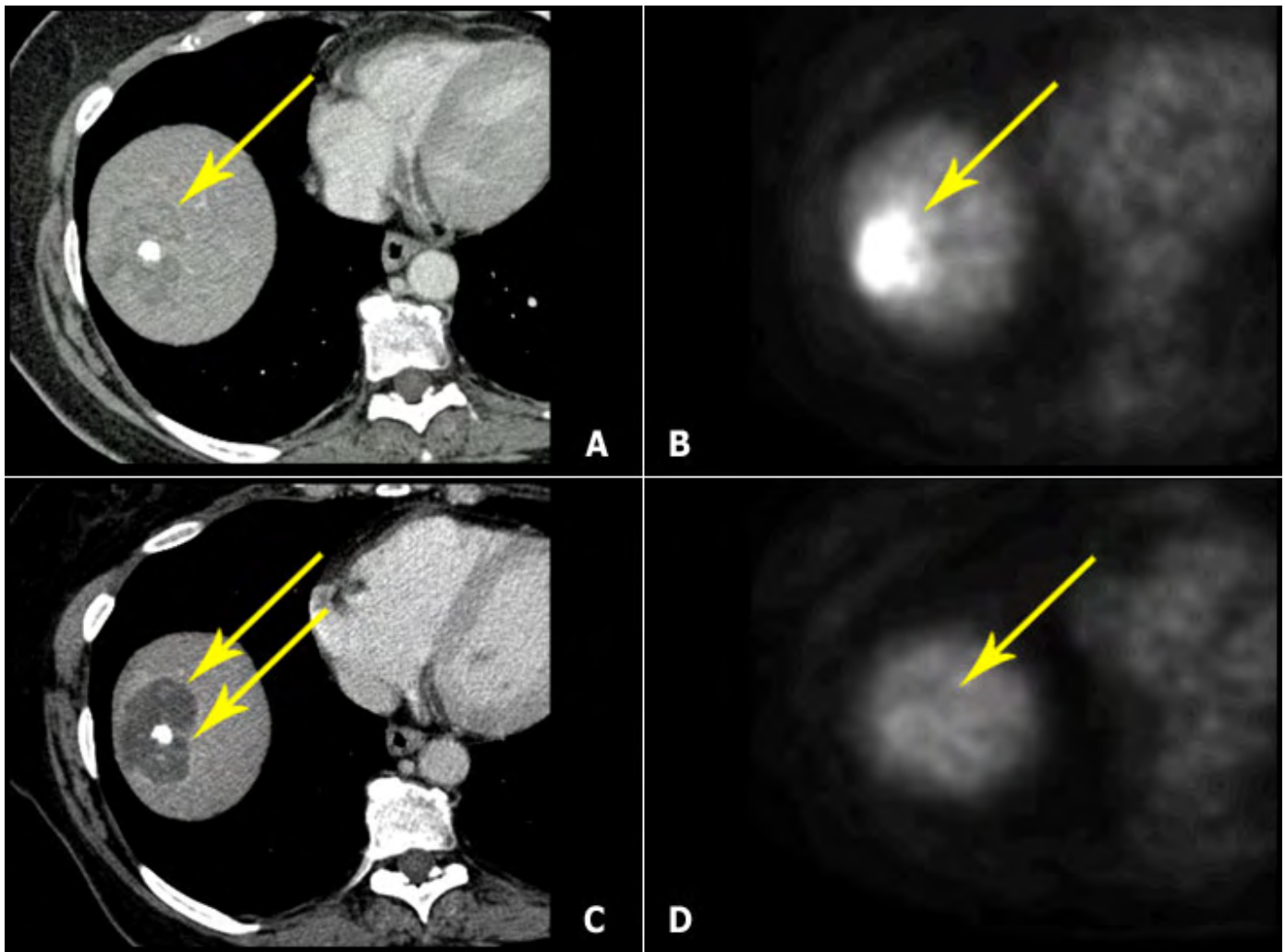


Figure 3. (A) Axial CT (pre-SIRT) of the liver in a patient with colon cancer shows metastasis (arrow) in segment 8 of the liver. (B) PET image of same patient showing high focal uptake (arrow) of ¹⁸F-FDG in the tumor. (C) CT image of same patient 6 weeks after treatment with SIRT showing complete necrosis of the tumor. (D) PET image of same patient, 6 weeks after treatment showing diminished uptake of FDG.

A PET/CT scan (Figure 3A and B) is performed to evaluate the extent of metastasis as well as to provide a baseline measure of metabolic activity of the tumors, which will be used to assess response to SIRT. If the PET/CT scan confirms that the metastases are confined to the liver or extra-hepatic disease is minimal, angiography will be used to assess the patient's hepatic artery and celiac axis. The gastroduodenal artery and right gastric arteries are generally coil-embolized at this time to prevent reflux of the resin microspheres (Figure 4). Then, ^{99m}Tc -macro aggregated albumin (MAA) are infused into the proper hepatic artery for perfusion scintigraphy. MAA particles are similar in size to SIR-Spheres[®] and provide information about blood flow from the hepatic artery, in particular to the lungs and abdominal organs (Figure 5). If more than 20% of the radioactivity reaches the lungs via hepatopulmonary shunting, SIRT is contraindicated because of the risk of developing radiation pneumonitis. If 10-20% reaches the lungs, it is possible to perform SIRT with a reduced dose of ^{90}Y . If <10% reaches the lungs, the procedure can be conducted using the standard protocol.

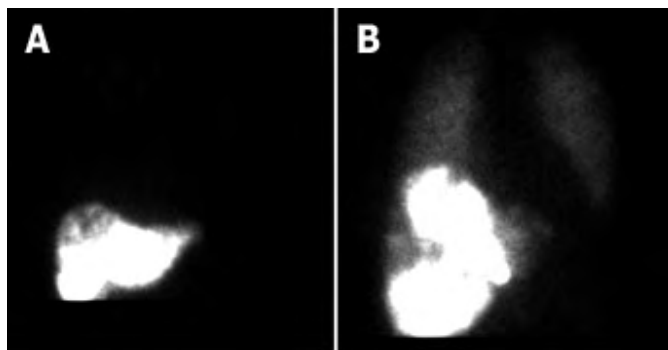


Figure 4. Scintigraphy images of the thorax and the liver following intra-arterial administration of ^{99m}Tc -Macroaggregated albumin in to the proper hepatic artery prior to SIRT procedure. **A** In one patient the hepatopulmonary shunt is less than 5%. **B** In another patient the hepatopulmonary shunt is >20%, which makes the patient ineligible for SIRT.

The Procedure

SIRT is carried out in close coordination of an interventional radiologist who plans and performs the procedure, an oncologist who manages the patient's care, a nuclear medicine specialist who is authorized to administer the dose, a nuclear pharmacist who estimates the dose needed, prepares, and calibrates the preparation, and a radiation safety officer. For each procedure, the SIR-Spheres[®] are ordered from the manufacturer in Australia, flown to the U.S.A. and are delivered to MGH on the morning of the procedure. Patients are not allowed to eat or drink anything for 6 hours prior to the procedure, which is performed under conscious sedation and local anesthesia at the catheter insertion site. Under image guidance, an angiographic catheter is inserted and placed in the proper hepatic artery. SIR-Spheres[®] are infused from a micro-catheter within the angiographic catheter to treat the entire liver. In some cases, if there are many small tumors scattered throughout the liver, two treatments can be given, with SIR-Spheres[®] into the right hepatic artery at one time and the left hepatic artery in a second treatment session. Once the infusion is completed, the microcatheter is withdrawn into the angiographic catheter prior to its removal to prevent unwanted deposition of radioactivity.

After the procedure is completed, patients are required to lie flat for 2-6 hours. If they experiences nausea, they will be given anti-emetics. Patients stay in hospital overnight for observation. Precautions to prevent unnecessary exposure to radiation include avoiding close contact with pregnant women and children for a few days following the procedure.

Complications

Low-grade fever, loss of appetite, lethargy, and fatigue are common for up to 6 weeks after the procedure. Acute abdominal/epigastric pain and/or nausea has been reported to occur in 30%. In one study, gastric ulcers were reported in 5% of patients. Unfortunately, radiation-induced ulcers do not heal well. Radiation-induced liver disease or pancreatitis is very rare.

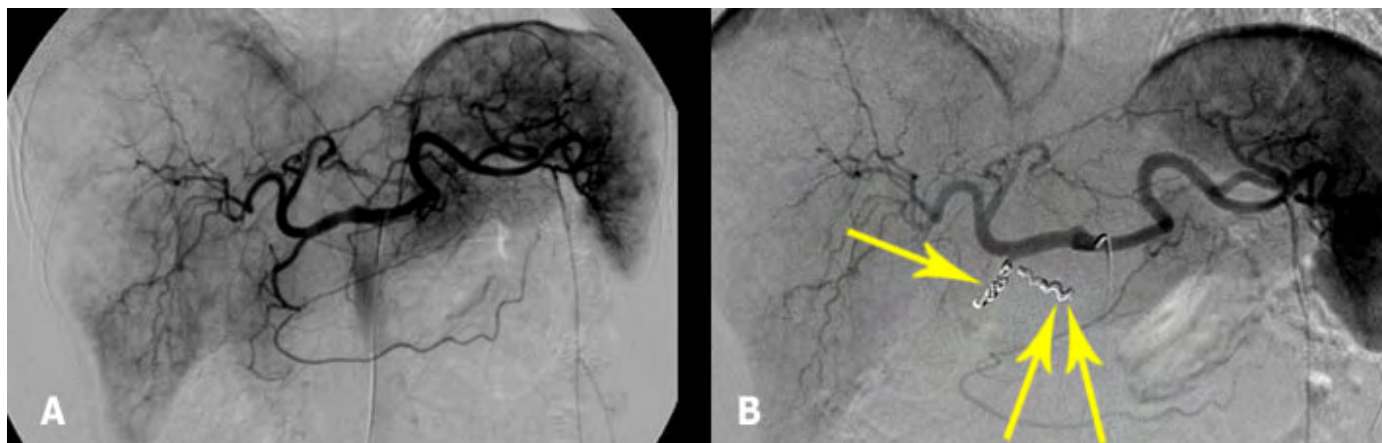


Figure 5. **A** Pre-treatment angiogram shows normal celiac artery. **B** Angiogram after coil embolization of the gastroduodenal artery (GDA) (single arrow) and right gastric artery (RGA) (two arrows) shows successful embolization with no flow in to these vessels. This is performed to prevent accidental reflux of SIR-Spheres[®] from the hepatic artery to the gut vessels.

Follow-up

PET is more sensitive than CT for the assessment of early response. Therefore, PET-CT imaging (Figure 3C and D), together with laboratory tests for tumor markers, is used to assess response 6 weeks after initial treatment and at subsequent 3-month intervals for the first year and every 6 months thereafter to detect recurrence or spread of disease. If liver tumors recur but there are no metastases elsewhere, it is possible to retreat with SIRT.

Scheduling

SIRT is only performed on the MGH main campus. An appointment with a vascular interventional radiologist to discuss this treatment may be scheduled by calling 617-726-8315.

Further Information

For further questions on SIRT or patient eligibility, please contact [Sanjeeva P. Kalva, M.D.](#), at 617-726-8314 of the Cardiovascular Division, MGH Department of Radiology.

We would like to thank Dr. Kalva and Lawrence S. Blazzkowsky, M.D., Medical Oncologist from the Hematology/Oncology Unit, Department of Medicine, for their advice on this topic.

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