



## Selective Internal Radiation Therapy

### **After completing this tutorial, attendees will be able to:**

- Explain how the concept of SIRT works
- Describe the physical appearance of the Y-90 Microspheres and state the approximate diameter of the particles
- Explain why the Microspheres are able to deliver a very high dose to liver tumors while preserving normal liver tissue
- Give a brief description of the treatment planning
- Explain why we must perform an MAA SPECT scan prior to the treatment
- Discuss the options if there is significant shunting to the lungs
- List several side effects of the procedure
- Describe the radiation safety issues associated with this procedure
- Identify the internal radiation dose absorbed by the patient during the procedure
- Know about insurance reimbursement for the procedure
- Identify 2 advantages to this procedure over all other therapeutic procedures for patients with tumors metastatic to the liver.

### **Topics to be covered**

- Concept of Selective Internal Radiation Therapy (SIRT)
- Science & Specifications of Y-90 Microspheres • Published Outcomes
- Patient Selection
- Treatment Planning
- Pre-Treatment Testing
- Treatment Issues
- Internal Radiation Dosimetry
- Administration Technique
- Side Effects
- Discharge

- Radiation Safety
- Clinical Studies
- Conclusions

**Two different manufacturers prepare Y-90 Microspheres. The similarities and differences between the two products are listed below:**

**Comparative Charts: Y-90 SIR-Spheres and Y-90 Theraspheres**

**SIMILARITIES**

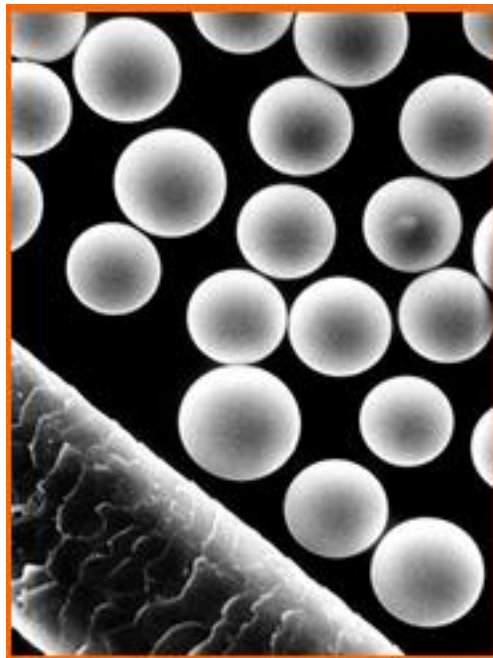
<b>Y-90 SIR-Spheres</b>	<b>Y-90 Theraspheres</b>
(average size 30-35 microns)	(average size 30-35 microns)
Labeled with Y-90	Labeled with Y-90
94% of rad dose delivered within 11 days	94% of rad dose delivered within 11 days
Provide targeted radiation with an average tumor dose of 280-380 Gy, a much higher than can be achieved with external beam radiation.	Provide targeted radiation with an average tumor dose of 280-380 Gy, a much higher than can be achieved with external beam radiation.
The normal liver dose is less than 80 Gy	The normal liver dose is less than 80 Gy
Maximum Beta Energy 0.93 MeV	Maximum Beta Energy 0.93 MeV
Half life 64.1 hr	Half life 64.1 hr
Avg penetration: 2.5 mm	Avg penetration: 2.5 mm
Max penetration: 11 mm	Max penetration: 11 mm
Distributed non-uniformly	Distributed non-uniformly

**DIFFERENCES**

<b>Y-90 SIR-Spheres</b>	<b>Y-90 Theraspheres</b>
Polystyrene resin microspheres	Glass microspheres
Low radioactivity per sphere (50 Bq)	High radioactivity per sphere (4,000 Bq)
Specific gravity of saline; low density	Specific gravity of glass > saline
40-60 Million spheres/dose	0.5-2 Million spheres/dose
Higher probability of occlusion	Lower probability of occlusion
Lower probability of administering prescribed dose	Higher probability of administering prescribed dose
Manufactured in Australia	Manufactured in Canada

## Specifications:

- Resin particles 20-40 microns in diameter (avg: 32 microns)
- Y-90 = pure beta emitter chemically bound
- Max tissue penetration is 11 mm (avg 2.5 mm)
- Half-life- 64.1 hours (~2.67 days)
- 94% of radiation dose is delivered within 11 days
- Radioactivity per sphere (50 – 4,000 Bq/sphere)
- Easily suspended in water-specific gravity of saline
- Slightly embolic
- Dose extracted from bulk individual dose
- Approximately 20-40 million spheres are delivered using a microcatheter that is well advanced into the arterial system.



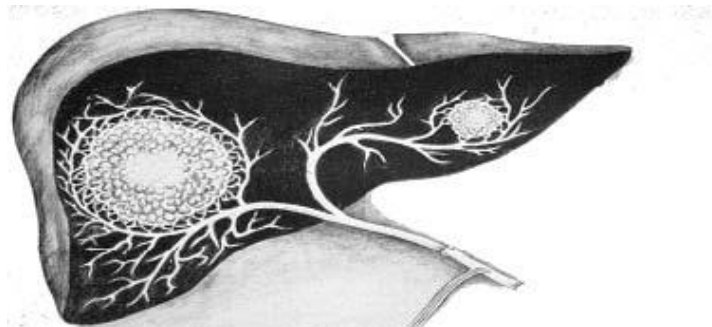
## Dose Administration

- The administration procedure is performed as an outpatient procedure. The patient can resume chemotherapy 4 weeks post treatment with SIRT.
- SIRT administration requires a coordinated multi-disciplinary team that includes:
  - Interventional Radiology
  - Radiation, Medical, Surgical Oncology
  - Nuclear Medicine, Radiochemist, Physicist, RSO
  - A designated program coordinator
- SIR-Spheres ® were approved by the FDA in March 2002 for Metastatic Colorectal Cancer Patients
- Under the terms of the Medicare Prescription Drug Improvement and Modernization Act of 2003 Medicare reimburses the hospital at 100% cost to charge ratio for the outpatient treatment
- Currently there are hundreds of US treatment centers
- Tens of thousands of patients have been treated in the USA and worldwide.

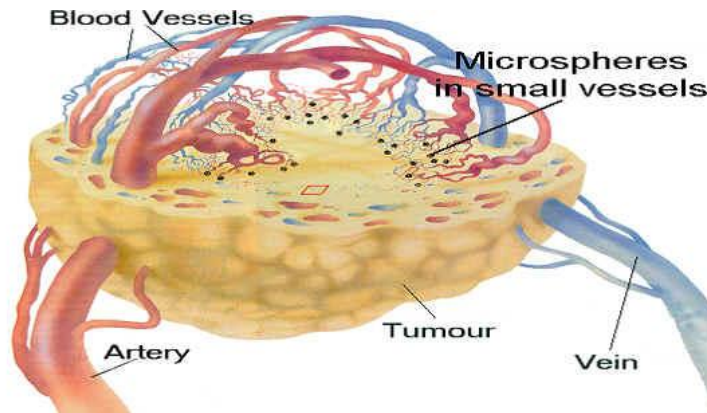
## Concept of SIRT

- To selectively target a very high radiation dose to all tumors within the liver while at the same time maintaining a low radiation dose to the normal liver tissue
- Y-90 Microspheres represent a new implantable radiotherapeutic device used to deliver Selective Internal Radiation Therapy or SIRT.
- While we tend to think of Y-90 Microspheres as a radiopharmaceutical, it is actually an implantable "sealed source" and was approved by the FDA as a device rather than as a radiopharmaceutical

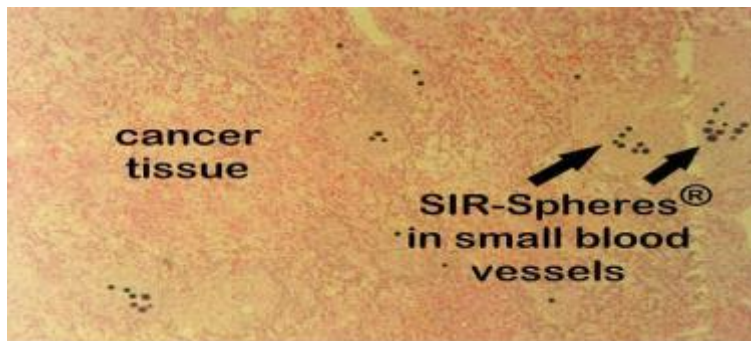
## Blood Supply to the Liver



- Dual blood supply to the liver – hepatic artery + portal vein
- Tumors >2 cm draw >80% blood from the hepatic artery
- Normal liver parenchyma draws >80% blood from the portal vein
- Hepatic artery supplies 90% of tumor; only 10% to normal liver



### Entrapment of SIR-Spheres in Vascular Bed



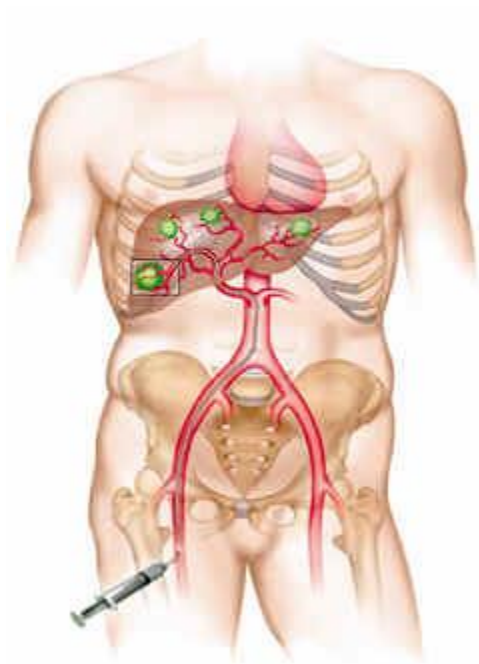
### SIR-Spheres Delivery Kit



## Administration Technique: Outpatient Admission



## SIR-Spheres Being Infused into the tumor



## PUBLISHED OUTCOMES

Phase III Randomized: SIRT + HAC FUDR

STUDY *	N = 70 patients	Time To Progression of Disease	SURVIVAL
HAC (FUDR) alone vs. SIRT + (FUDR)	34 HAC alone	9.7 months	<u>1 yr</u> - <u>2yr</u> 68% 72%
	36 SIRT + HAC	15.9 months  P<0.001	39% 29%

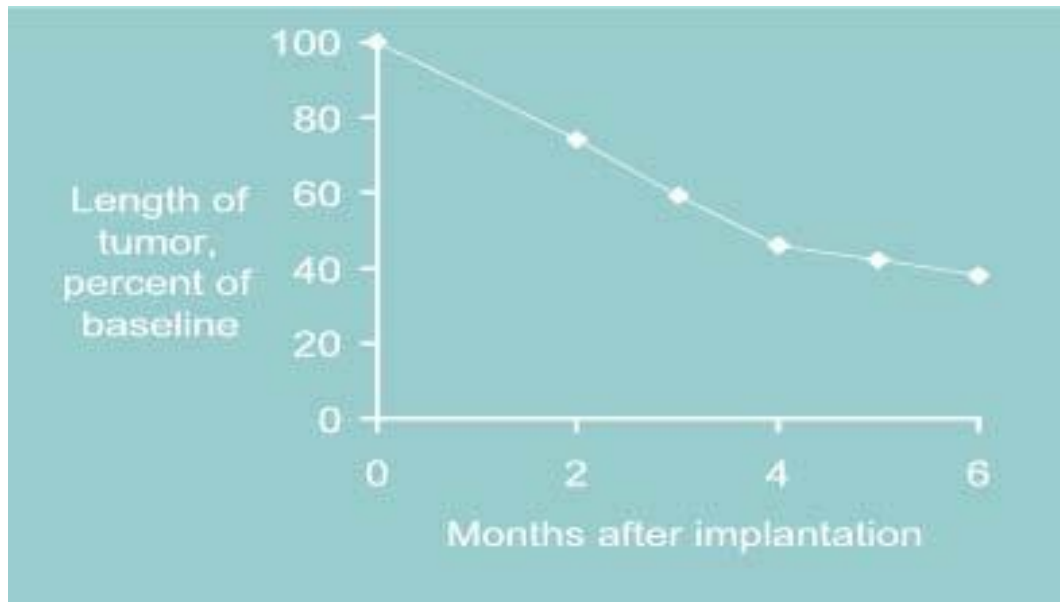
• FDA Study

•SIRT administered via an implantable port

•Previously untreated patients MCRC

\*Gray B, Van Hazel, G ASCO proceedings 2002 , Journal of Surgical Oncology -2004:88:78-85

These data represent the median tumor length based on outcomes from 226 tumors in 64 clinical trial patients.



## **PATIENT ELIGIBILITY CRITERIA**

- Liver dominant disease/Minor EHD
- Extensive angiogram work up/ some arterial embolization (GDA)
- Adequate hepatic function: Bilirubin should be no higher than 1.8-2.0
- Lung shunting less than 20% as determined by a MAA scan
- Patients should be taken off SYS chemotherapy 2-4 weeks prior to SIRT. SYS chemotherapy can resume 4 weeks after RX
- Not eligible for resection or transplant
- No other hepatic disease
- Adequate renal function- creatinine < 150 µmol/L
- Adequate hematological function- Granulocytes >1.5 x 10<sup>9</sup> /L, Platelets >100 x 10<sup>9</sup> /L
- CT scan showing unresectable liver malignancies within 28 days of SIRT

### **Patient Work-Up**

- CTHA
- MAA – lung shunting
- Patient workup procedure results in 5-10 % of patients not being eligible for SIRT

### **Diagnostic Angiography prior to placement of SIR Spheres**

- Technical issues: Groin /Arm / Type of Cath
- Anatomy: Replaced /Anomalous /Variants
- Selective / super-selective
- Portal vein patency
- Porto-venous shunts
- Coil embolization of GDA and RGA to prevent inadvertent spilling

### **PRE-TESTING- 1st Patient Outpatient Admission**

- Chest x-ray
- Triple Phase CT Scan of abdomen, chest and pelvis
- Abdominal/pelvic ultrasound and bone scan?



- PET Scan/PET CT
- Baseline liver function testing to determine the extent of liver damage/dysfunction
- Diagnostic mesenteric angiography for vascular mapping

Determines hepatic arterial anatomy

- Assessment of variants in vascular anatomy

Assesses risks of complications

- Shunt through tumor vascular bed to lungs
- Non-target embolization to adjacent organs

Can convert a "non-candidate"

### ■ Prophylactic embolization of branches to GB, GI tract, pancreas

#### Assessment of Anomalous Arteries

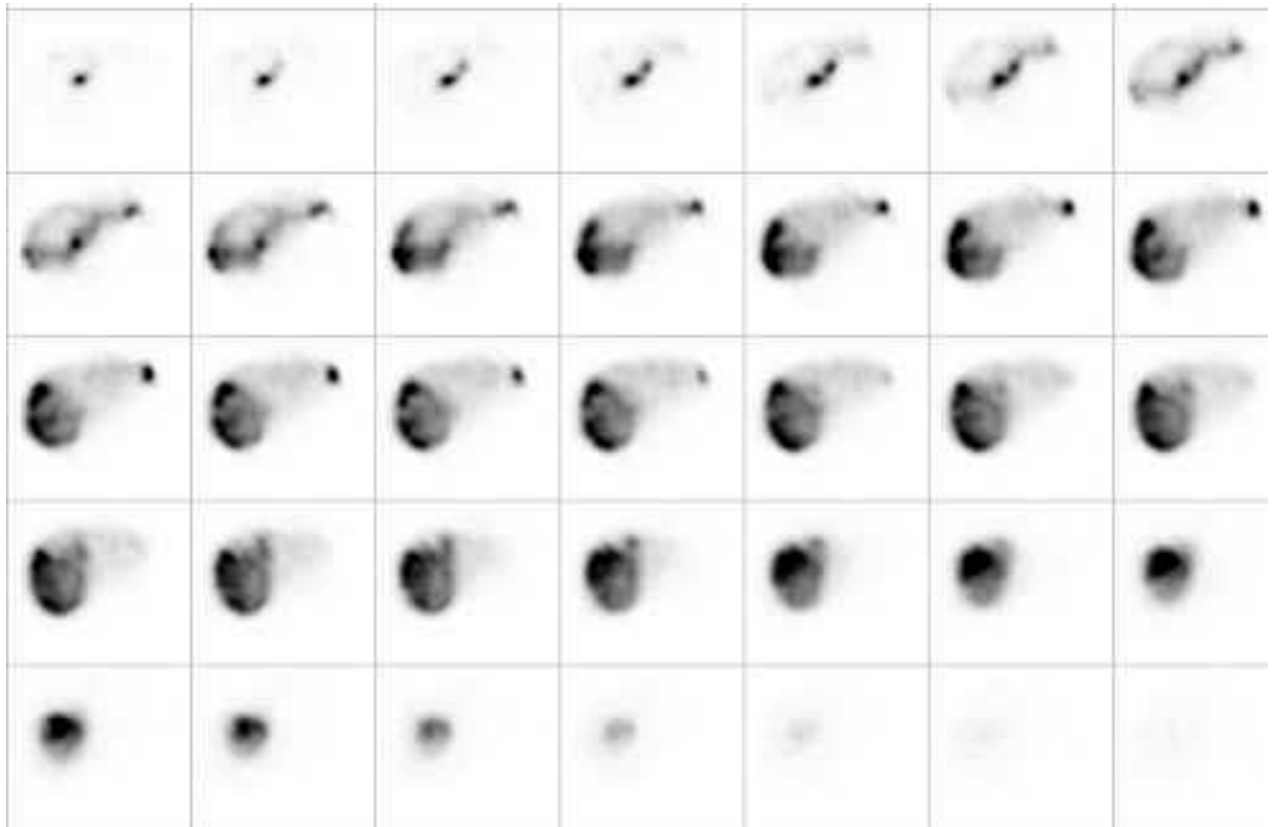
- 50% of patients have aberrant arteries supplying the liver
- 15% of patients have aberrant arteries from liver supplying the gut
- Variant hepatic anatomy: Covey et al, Radiology, 2002; 224; 542-547

#### MAA Shunt study

Tc-99m MAA STUDY: to determine pulmonary shunting that could result in non-targeted delivery to gastrointestinal tract

**Maximum 20% shunting as this will deliver a total cumulative dose to the lung of 30 Gray - maximum tolerable dose of lungs**

# MAA SPECT



<b>Lung Shunting- MAA</b>		
<b>Admin Activity: GBq</b>	<b>Lung Shunting %</b>	<b>Lung Radiation Dose: Gray</b>
<b>1</b>	<b>10%</b>	<b>5</b>
<b>1.5</b>	<b>10%</b>	<b>7.5</b>
<b>2</b>	<b>10%</b>	<b>10</b>
<b>2.5</b>	<b>10%</b>	<b>12.5</b>
<b>3</b>	<b>10%</b>	<b>15</b>
<b>1</b>	<b>15%</b>	<b>7.5</b>
<b>1.5</b>	<b>15%</b>	<b>11.25</b>
<b>2</b>	<b>15%</b>	<b>15</b>
<b>2.5</b>	<b>15%</b>	<b>18.75</b>
<b>3</b>	<b>15%</b>	<b>22.5</b>
<b>1</b>	<b>20%</b>	<b>10</b>
<b>1.5</b>	<b>20%</b>	<b>15</b>
<b>2</b>	<b>20%</b>	<b>20</b>
<b>2.5</b>	<b>20%</b>	<b>25</b>
<b>3</b>	<b>20%</b>	<b>30</b>
<b>If &gt;20%, do not treat</b>		

# DOSIMETRY

## Empiric Method- Based on Clinical Experience

Estimated Degree of Tumor Involvement in the Liver	Recommended Y-90 Dose for Treatment
>50%	3.0 GBq
25-50%	2.5 GBq
<25%	2.0 GBq

Note: Dose reduction is required if shunting to the lungs is greater than 10%

For 10-15% shunt, 20% dose reduction

For 15-20% shunting, 40% reduction

For shunting > 20%, do not administer Y-90 Microspheres

## BSA Method-

### Based on Body Surface Area and % tumor involvement

$$\text{Activity of Y-90 Microspheres (GBq)} = (\text{BSA} - 0.2) + \frac{\% \text{ tumor involvement}}{100}$$

For example, if tumor involvement = 30% and BSA = 2.0 m<sup>2</sup>, then

$$\text{Activity of Y-90 Microspheres (GBq)} = (2.0 - 0.2) + \frac{30}{100} = 1.8 + 0.3 = 2.1 \text{ GBq}$$

If whole liver dose = 2.1 GBq, then

Right lobe = 60% x 2.1 = 1.26 GBq and

Left lobe = 40% x 2.1 = 0.84 GBq

## TREATMENT PLANNING

### Treatment Algorithm:

- Initiate insurance certification process
- Consider pre-SIRT PET-CT (volumetric)
- Diagnostic mesenteric angiography
- MAA Shunting Study
- Joint treatment plan & calculation of dose (IR, Nuclear Med, Radiation Oncology)

Lobar vs whole liver ?

### SIRT Side Effects:

- Pain during the administration due to embolic effect of the spheres
- Nausea – anti-nausea medication is needed
- Lethargy – for 1-2 weeks after treatment, will subside with time and is a normal response to abdominal radiation
- Gastritis – due to reflux of spheres during administration

### Exposure:

- Bremsstrahlung radiation is typically 15 mSv per Gbq at 15 cm from the patient's right side (initially)

### Post – Treatment

- 23-hour hospital stay
- Single use room or low traffic area
- Non-pregnant nursing staff /visitors
- Nursing from left hand side of patient
- Minimize visitor number and time
- Shielding unnecessary

## Discharge Instructions

- Augmentin 500 mg or Cipro 500 mg for 5 days
- Anti-nausea suppositories
- Panadol Forte
- 8 glasses of water per day
- Make contact if nauseous/abdominal pain/fever greater than 102°F
- Resume light activity as soon as you feel like it

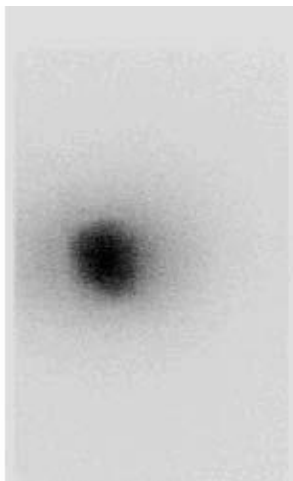
## **CLINICAL STUDIES**

- **> 20% of all tumors will clinically disappear**
- **Median time to elimination is 6 months**
- **Largest tumor to be eliminated had a baseline length of 100 mm**
- **Median reduction, irrespective of size, is ~ 60% (tumor 40% of baseline length)**
- **Largest linear reduction: 170 mm to 62 mm**

## **Post Treatment Imaging**

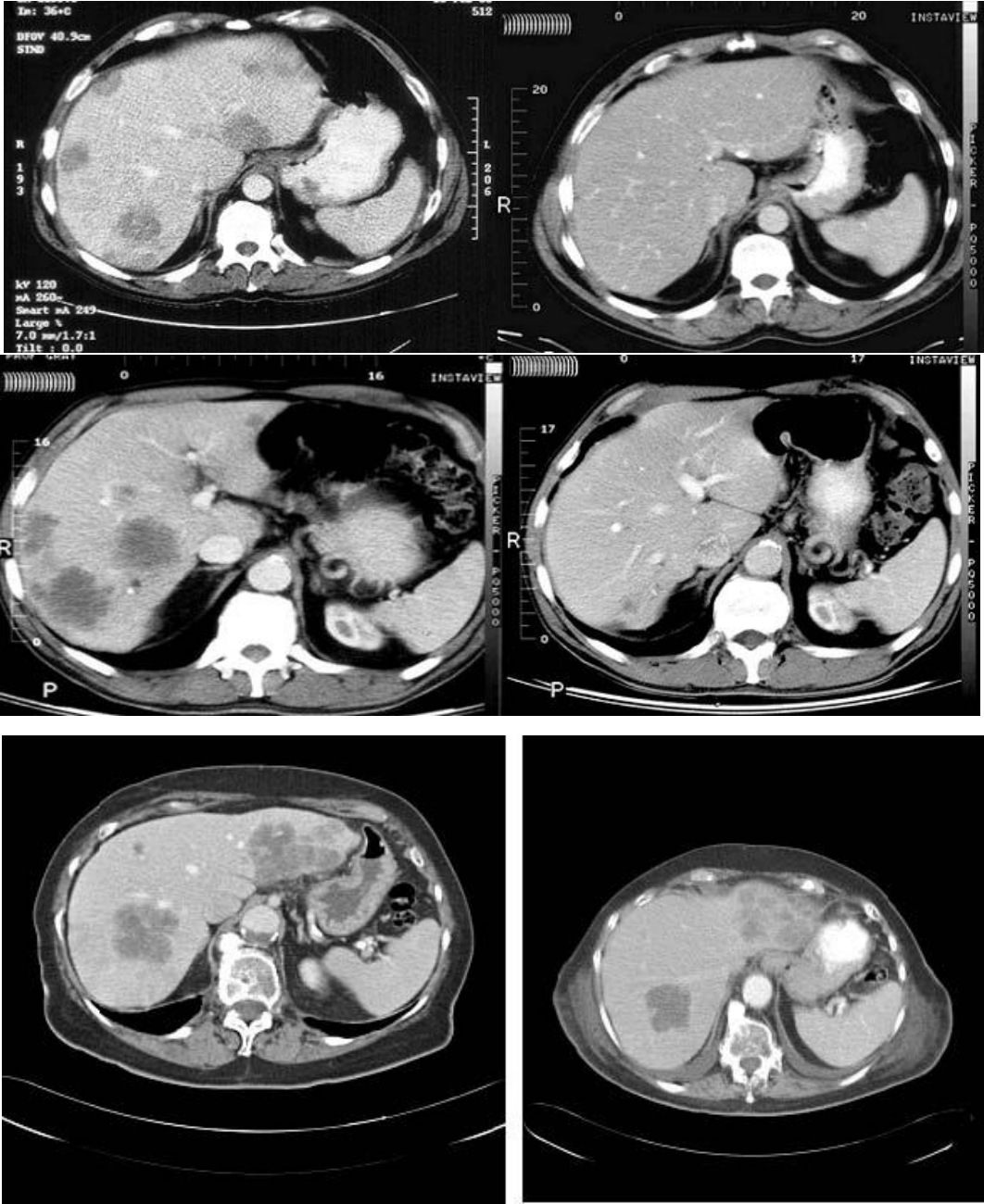


Pre Treatment-  
Tc-99m MAA



Gamma Image-  
Bremsstrahlung

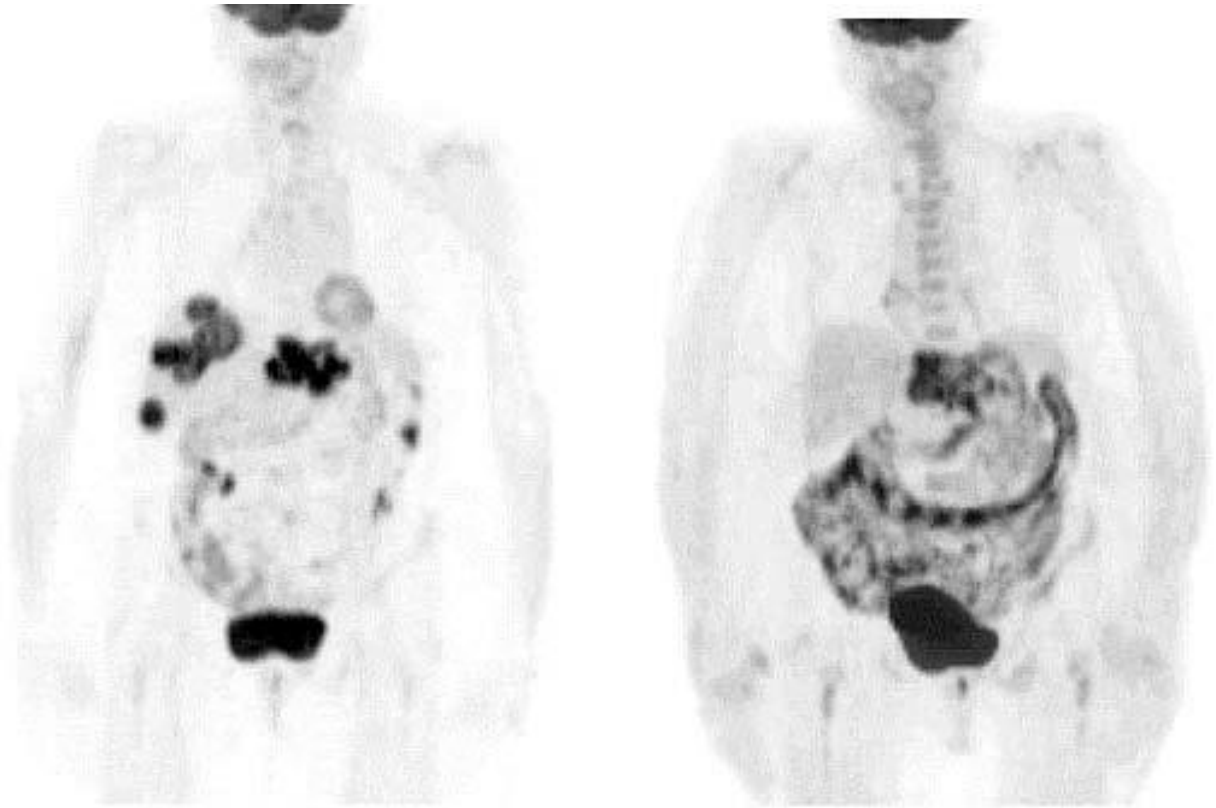
**Liver Metastases Derived From Colorectal Cancer – CT Scans**



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**Mets- Treated: Right Lobe Only  
CT Scan Before and After SIRT**

**MCRC- Treated: Right Lobe Only**  
**PET Scan Before and After SIRT**



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