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# Selective internal radiation therapy: An emerging treatment for hepatorectal cancer

**Maulesh Vyas[1]*, Nisha Upadhyay[1], Atanu Kumar Behera[1], Krunali Thakkar[2], D.B.Meshram[2]**

**[1]Department of Pharmaceutics, Pioneer Pharmacy Degree College, Vadodara, Gujarat, (INDIA)**

**[2]Department of Quality Assurance, Pioneer Pharmacy Degree College, Vadodara, Gujarat, (INDIA)**

**E-mail : mauleshv@gmail.com**

## ABSTRACT

The paper has reviewed the use of Selective Internal Radiation Therapy (SIRT) using SIR-Spheres, which is a therapeutic 'device' for the treatment of non-resectable hepatic metastases secondary to colorectal cancer in the absence of extrahepatic metastases. SIRT involves a single delivery of Yttrium$^{90}$ micro-spheres in the hepatic artery. Preferential uptake is achieved into liver tumors, because of their predominant hepatic arterial blood supply. The treatment is well tolerated and has been documented internationally to achieve response rates of around 90% in patients with extensive colorectal cancer (CRC) liver metastases. The product obtained FDA approval in the USA in 2002. Unlike other ablative therapies being applied to non-resectable liver tumors, SIRT is indicated even in patients with an extensive burden of liver tumor. Indications, dosing schedules and expected outcomes will be better defined.



## KEYWORDS

Selective internal radiation therapy;
Metastases;
Colorectal cancer;
Yttrium$^{90,}$ grey unit.

## INTRODUCTION[1-12]

The options and possibilities for the management of colorectal liver metastases have changed immensely over the last 25 years[1].Operative techniques and the knowledge to support liver resection have developed alongside a number of ablative methods for the management of non-resectable liver metastases including cryotherapy[2], radiofrequency ablation[3] and laser electrocoagulation[4]. Internal Radiation Therapy (SIRT) using SIR-spheres, which is a therapeutic 'device' for the treatment of non-resectable hepatic metastases secondary to colorectal cancer in the absence of extrahepatic metastases and in combination with hepatic arterial chemotherapy or systemic chemotherapy[5-7]. SIR-Spheres are intended for implantation into malignant liver tumours for the purpose of selectively delivering high doses of ionized radiation to the tumour[8]. The technique entails the delivery of yttrium$^{90}$ microspheres into the hepatic artery to obtain a degree of selective uptake into hepatic tumours, by virtue of the predominant hepatic arterial supply to tumours as opposed to the predominant portal venous supply to normal liver parenchyma[9-11]. In this way large and lethal doses of radiation can be delivered to tumors while ensuring that the dose received by the non-tumorous areas of the liver is tolerated without the development of serious or even fatal radiation hepatitis[12].

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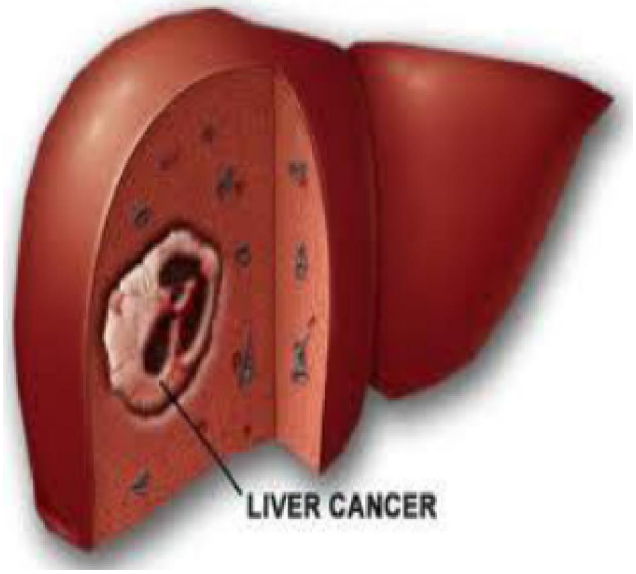


**Figure 1: Liver cancer[46]**

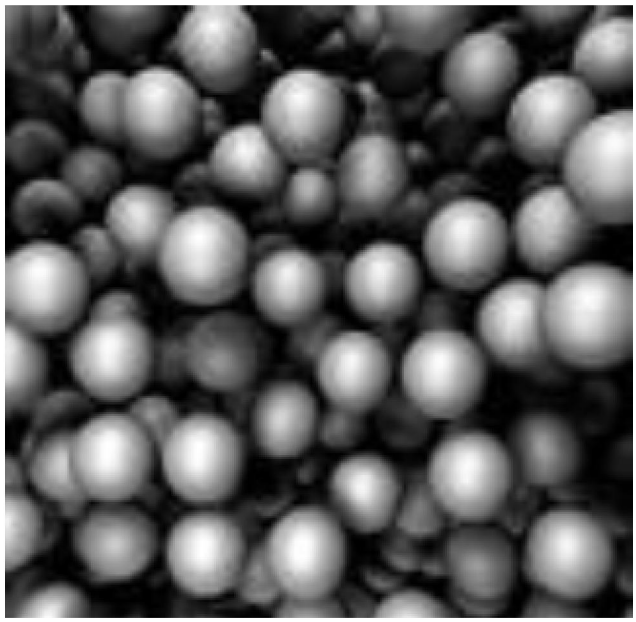

**Figure 2: SIR-Spheres[47]**

## BACKGROUND[13-18]

External beam radiation has not found an appreciable place in the management of liver tumors because the liver is poorly tolerant of radiation therapy. Whole-Liver doses in excess of 30 Gy may cause fatal radiation hepatitis, which is characterized by the development of portal hypertension, ascites, progressive liver failure and death as a result of a Veno-occlusive-type lesion[13-14]. Yttrium90 is a high-energy, pure β-emitter with a half-life of 64 hours and maximum tissue penetration of 11 mm, which makes it very suitable for treatment of liver tumors[15-17]. It is relatively straightforward to use, with few issues relating to radioprotection for the patient, family or attending staff. The microspheres are approximately 35 μm diameter, which means that they become permanently trapped at the arteriolar end of the capillary bed. The number of microspheres administered is such that the procedure has little or no devascularizing component. Yttrium$^{90}$ microspheres are commercially available at the present time. The first, SIR-spheres® (Sirtex Medical Ltd, Sydney, Australia), were fully approved by the FDA in the USA for use in colorectal cancer (CRC) liver metastases in March 2002 and have more recently been similarly approved for use throughout Europe. They are resin microspheres, and a typical dose involves administration of 20–40 million microspheres[18].

## RADIOACTIVE MICROSPHERES[19-21]

Currently two types of radioactive microspheres are available which can be used for primary and metastatic liver diseases. They both contain Yttrium$^{90}$ but their carrier molecule is different. Average activity per sphere is known allowing delivered dose to be calculated. Yttrium$^{90}$ is predominantly beta emitter with an average tissue penetration of 10 mm. It becomes inactive after 10 days of radioembolisation[19].

- 90Y glass microspheres (Theraspheres, MDS Nordian, Canada) are glass microsphere with diameter 25+10 micrometer. They embolize at arterial level.
- 90Y resin based microspheres (SIR-spheres®Sirtex Medical Ltd, Sydney, Australia) with a diameter of 29-35 micrometer.
- SIR-sphere have much lower specific activity per bead, meaning that many more beads require than Theaspheres toachieveethe same amountt of radiation. This leads much greater embolic effects with the use of SIR-spheres

## TECHNIQUE FOR ADMINISTRATION[22-26]

SIR-Spheres are intended for implantation into malignant liver tumors for the purpose of selectively delivering high doses of ionizing radiation to the tumor. This is accomplished by injecting the SIR-Spheres into the hepatic artery. This requires Catheterization of the hepatic artery either via a trans-femoral catheter or a

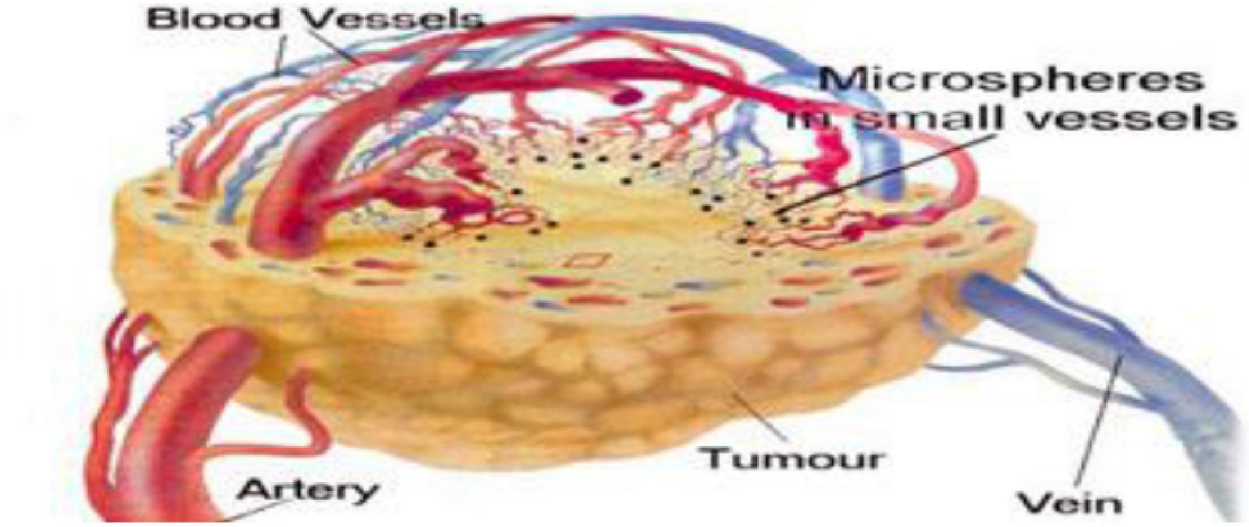


**Figure 3 : Entrapment**

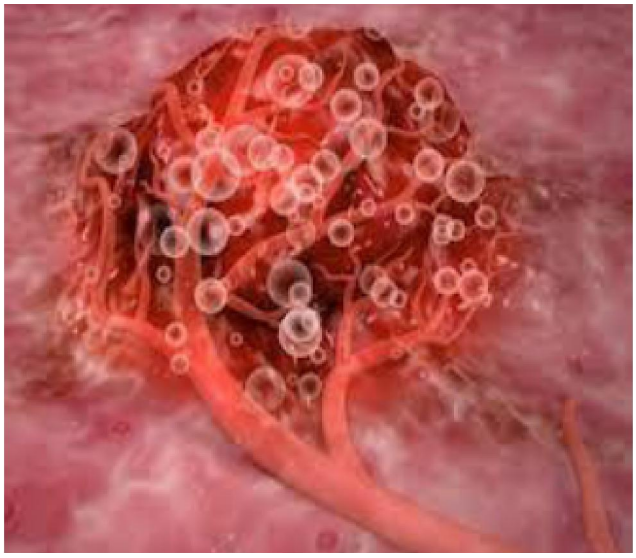

**Figure 4 : SIR-Sphere[49]**

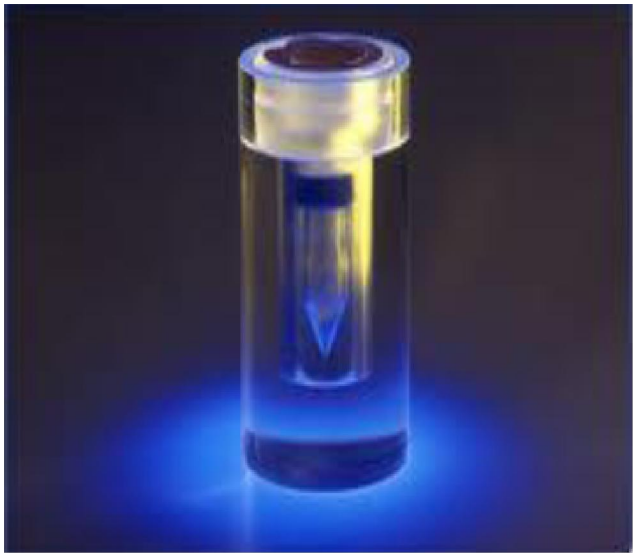

**Figure 5 : Therasphere[50]**

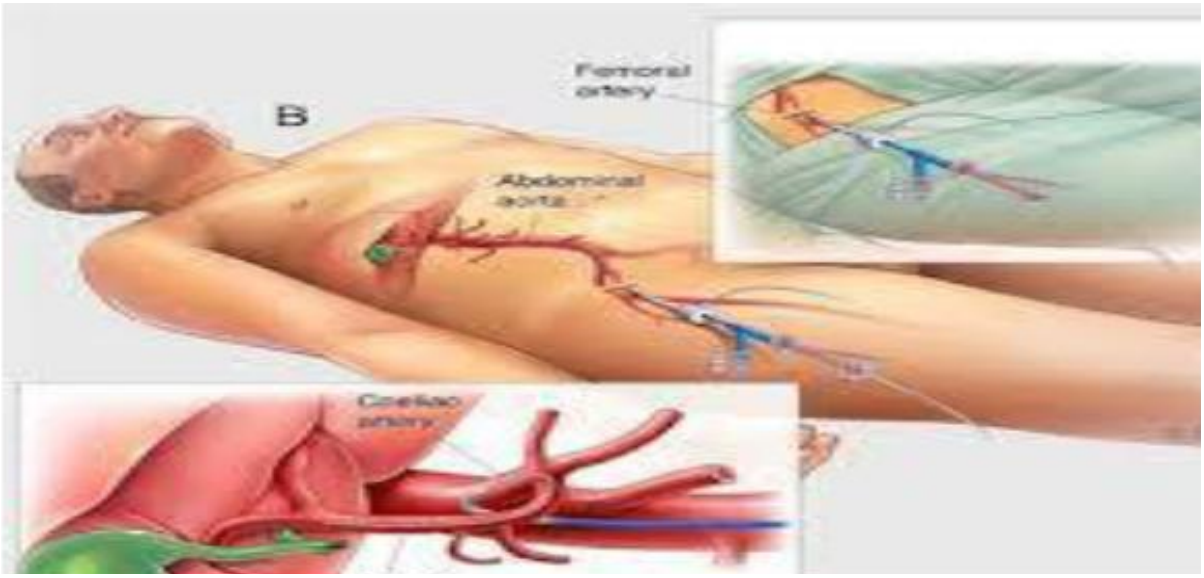


**Figure 6 : SIR-Spheres administration[51]**

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permanently Implanted hepatic artery port with catheter[22-23]. Following embolisation into the hepatic artery by catheter, SIR-Spheres become Concentrated in the microvasculature of liver cancer where they have a local Radiotherapeutic effect. Some limited concurrent damage to healthy tissue is caused by radiation that escapes tumor boundaries and from SIR-Spheres that fail to become Embedded in tumors. Following decay of the yttrium-90, the inert resin microspheres remain implanted in tissue. As tumors within the liver derive their blood supply almost exclusively from the hepatic artery, the SIR-Spheres are preferentially delivered in greater amounts to the tumor rather than the normal liver parenchyma which is supplied by both the hepatic artery and the portal vein[24-26].

## PATIENT COMPLIANCE[27-32]

The treatment is generally very well tolerated, although approximately one-third of patients will experience severe pain and nausea towards the end of the procedure. These symptoms are managed with intravenous narcotic analgesia and anti-emetics and usually subside within 24 hours. Most patients will experience marked lethargy and anorexia after the procedure for 3–6 weeks[27-29]. No other specific problems are usually encountered. While hepatic artery catheterization is a minimally invasive technique relative to the laparotomy required for port and pump implantation, complications associated with repeated arterial puncture and poor patient acceptance due to frequent catheter migration and the need for hospitalization and confinement to bed, have limited its use[30-32].

## TOXICITY[33-34]

Colorectal cancer indicates that the toxicities of intrahepatic chemotherapy may include sclerosing cholangitis (10%), which may be fatal in some cases, chemical gastritis or cholecystitis (10%), peptic ulceration (5%), and diarrhoea (5%)[33-34].

## DOCUMENTATION OF TREATMENT[36]

Reporting should be in accordance with the ACR Practice Guideline for Communication: Radiation Oncology or the ACR–SIR Practice Guideline for the Reporting and Archiving of Interventional Radiology Procedures, with the addition of:

1. Specification of the activity of yttrium-90.
2. Target volume: whole liver, right or left lobe, or segment.
3. Final activity delivered.
4. Any evidence of target embolization.
5. Any evidence of nontarget embolization.
6. Condition of patient on discharge.
7. Follow-up clinical visits planned.
8. Follow-up laboratory/radiological examinations.
9. Final disposition of patient.

## AFTER THE PROCEDURE[37-40]

The recovery time after the procedure varies between 4 to 6 hours. You will need to lie flat and keep your leg (or arm) still and straight. Moving too soon after the procedure may cause bleeding at the puncture site. The IV Cannula will be removed after you have recovered. Most patients experience Post embolisation Syndrome which includes pain, nausea, vomiting and fever. It is due to the blood supply to the treated area being cut off. You will be able to go home once your pain and nausea have settled, usually within 2 days. It is normal to have a fever for up to a week after the procedure. Loss of appetite and fatigue are common and may continue for two weeks or longer. Staff will discuss with you the need to restrict your activities at home for up to 5 days. Follow these instructions carefully.

## RECENT ADVANCES

SIR-SPHERES are also useful in the treatment of the type of liver metastases coming from the different part of the body. The recent advances in this treatment which are as follows.

**TABLE 1**

| Sr. No. | Diseases | References | Median survival |
|---|---|---|---|
| 1 | Breast cancer | 41 | 86% alive in 14 months |
| 2 | Cholangiocarcinoma | 42 | 9.3 months |
| 3 | Hepatocellular carcinoma | 43 | 16 months |
| 4 | Endocrine tumors | 44 | 70 months |
| 5 | Ocular melanoma | 45 | 80% in 1 year |

## CONCLUSION

The selection of internal radiation therapy has added an effective treatment for primary and secondary liver tumors. It is well tolerated and also has very less adverse effects that can be effectively minimized by proper preparation, dose adjustment and administration. Despite being regarded as non-curative, it has been associated with improved survival, reduction in tumor marker, and regression in the number and size of lesions. Follow up with imaging is necessary to access response of therapy.

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