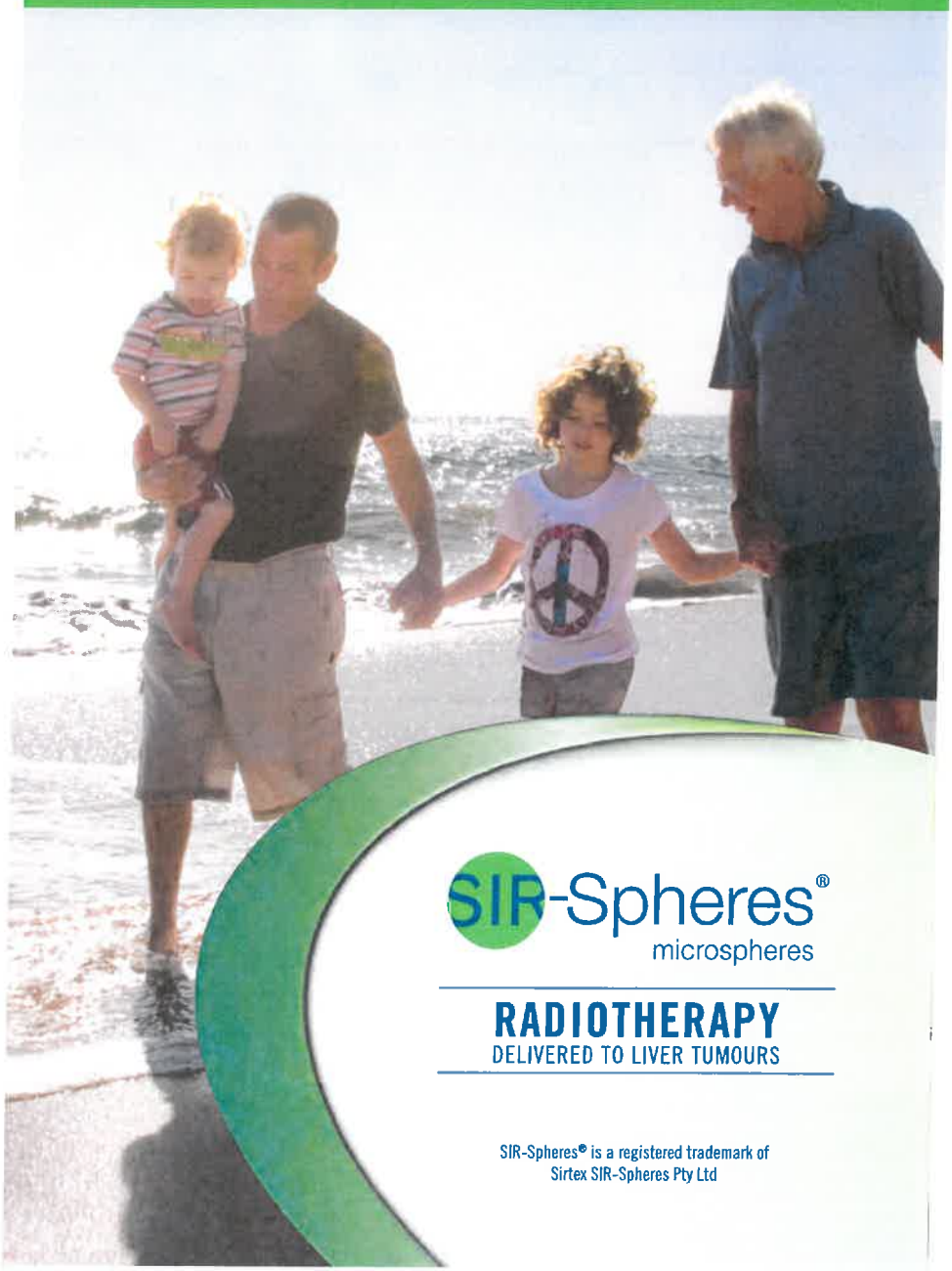
SIRTeX

A Patient's Guide:

Selective Internal Radiation Therapy (SIRT) for liver tumours using SIR-Spheres microspheres



SIR-Spheres® microspheres

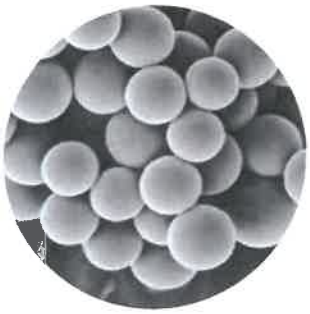
RADIOTHERAPY
DELIVERED TO LIVER TUMOURS

WHAT IS SIRT?

Selective Internal Radiation Therapy (SIRT) is a way to use radiotherapy to treat liver cancer that cannot be removed with surgery or local ablative techniques such as radiofrequency ablation (which means destroying using radio waves). This means the radiation is delivered into or close to the tumour(s), rather than delivered from outside the body.

WHAT ARE SIR-SPHERES MICROSPHERES?

SIR-Spheres microspheres used in SIRT are extremely small (20-60 microns; about one-third the diameter of a strand of hair) resin beads which contain the radioactive substance yttrium-90 (Y-90).



Electron micrograph of SIR-Spheres microspheres

Because of their small size, the microspheres enter the small blood vessels of the tumour. Radioactivity is delivered directly to the tumour tissue.

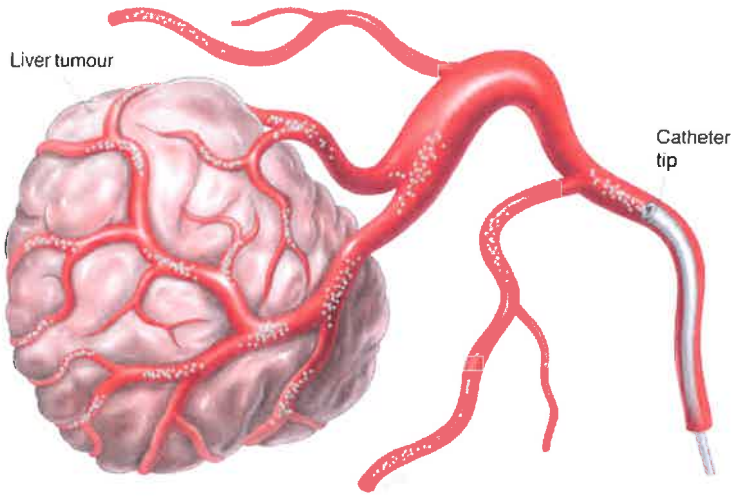
HOW DOES SIRT WORK?

Radiation is an effective way to destroy tumour tissues and is used widely in cancer treatment.

However, the organs and tissues in the body are sensitive to radiation and may also be damaged by radiation treatment. Thus, conventional radiotherapy

(external beam radiation delivered from outside the body) can only be given to limited areas of the body.

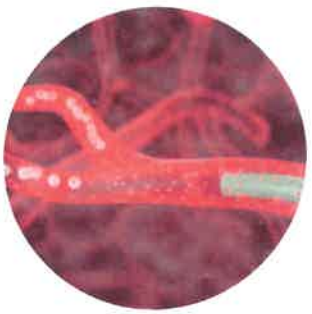
The liver can only tolerate small doses of external radiotherapy. Because SIRT targets the tumour(s), it can deliver a larger dose of radiation directly over a longer time than is possible with external beam radiation.



Liver tumours treated with SIR-Spheres microspheres

HOW DO SIR-SPHERES MICROSPHERES WORK?

Due to the unique blood supply of the liver, SIR-Spheres microspheres can be delivered directly into the liver tumours. This targeted treatment allows maximum radiation doses to be administered to the liver while reducing exposure to the remaining healthy tissue.



SIR-Spheres microspheres flow with the blood

The microspheres are small enough to flow through the hepatic arteries, but they are too large to

pass through the small blood vessels within the tumour, where they become permanently lodged in the tumour bed.

WHO IS SIRT SUITABLE FOR?

SIRT is only suitable for patients who have liver tumours where either the liver is the only site of disease or the liver is the major site for disease. SIRT has no effect on tumours outside the liver.

Before SIRT can be offered as a treatment option for patients, there are a number of other factors that have to be considered. Most importantly, you need to have a sufficiently healthy liver that is working satisfactorily. This is usually determined by a simple blood test.

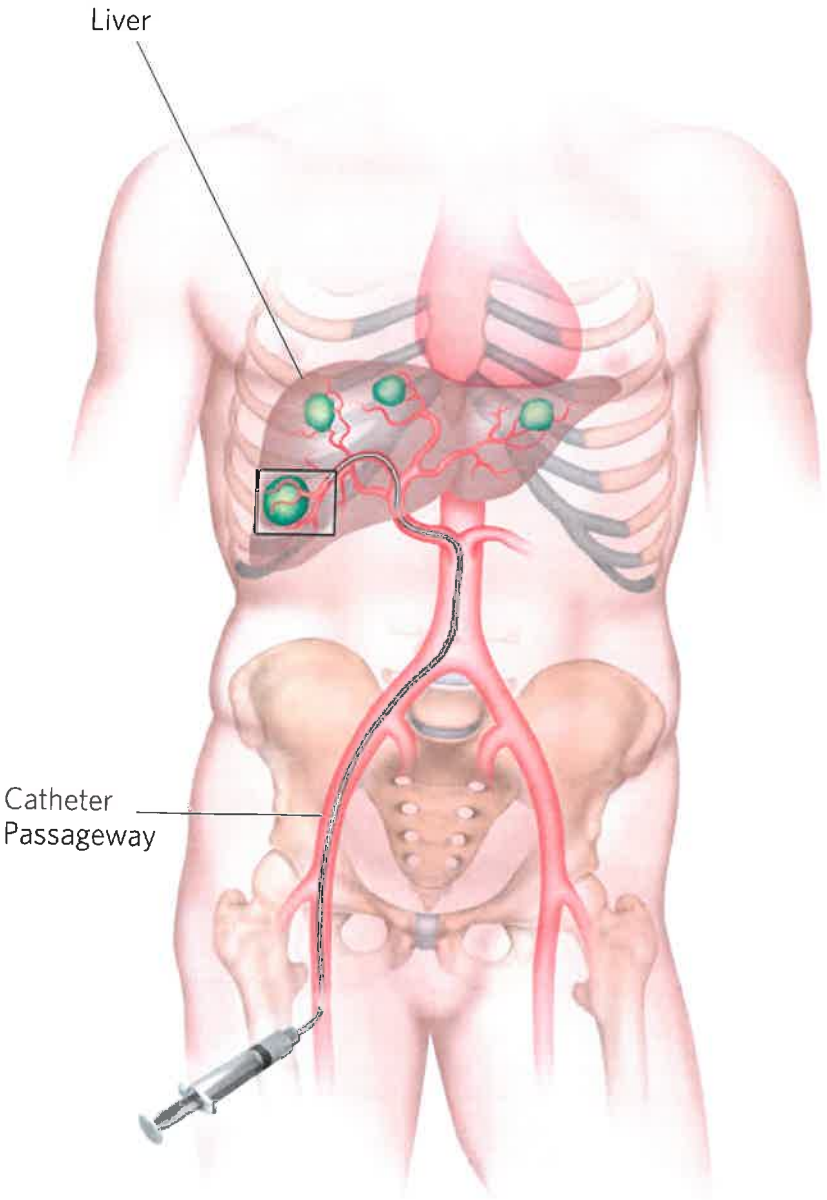
WHO PERFORMS THE SIRT PROCEDURE?

The SIRT procedure is conducted by a medical team that includes a specialist known as an interventional radiologist, together with other specialists trained to work with radiation.

HOW ARE SIR-SPHERES MICROSPHERES ADMINISTERED?

The interventional radiologist makes a small puncture, usually into the femoral artery near the groin. A small flexible tube, known as a catheter, is then guided through the artery into the liver. The SIR-Spheres microspheres are administered

through this catheter. The whole procedure may take about 90 minutes. You will be sleepy during the procedure but you will be able to communicate with your treating doctor and the team.



Administration of SIR-Spheres microspheres

WHAT WILL MY TREATMENT TEAM DO BEFORE ADMINISTERING SIRT?

Your treatment team will want to know about your previous cancer history and any other medical conditions. They will then conduct a number of initial tests to ensure that it is possible for you to receive SIRT safely. Normally patients will undergo two procedures under conscious sedation. Both procedures will include a radiology procedure known as an angiogram.

The purpose of the first angiogram or mapping is to prepare your liver for the SIRT treatment. During the mapping procedure your interventional radiologists will block (embolise) the vessels to minimise the potential for the microspheres to travel to areas outside your liver (e.g. the stomach or intestine). You will also receive a small amount of radioactive "test beads" to check any amount of flow of beads from the liver to the lungs.

Assuming that the results of these initial tests are acceptable, the dose of SIR-Spheres microspheres will be determined. The SIR-Spheres microspheres will then be administered during a second procedure which is typically conducted one to two weeks after the initial tests are completed.

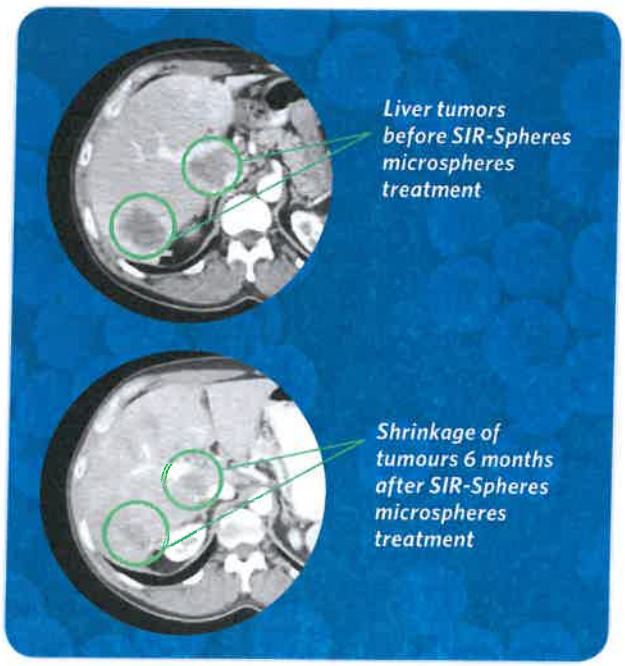
SIRT administration flowchart

WILL I HAVE TO STOP MY CHEMOTHERAPY TREATMENTS TO RECEIVE SIRT?

Generally, most patients' chemotherapy is stopped two weeks before the SIRT procedure and for two weeks after. However, your oncologist will determine if your chemotherapy needs to be stopped during this time.

WHAT ARE THE POTENTIAL BENEFITS OF SIR-SPHERES MICROSPHERES?

Clinical data show that when used in combination with chemotherapy, SIR-Spheres microspheres may shrink patients' liver tumours from colorectal cancer more than chemotherapy alone, improve quality of life and increase life expectancy. For a small number of patients, treatment can cause sufficient shrinkage of the liver tumour to permit its removal by surgery at a later date. In patients whose liver tumours are no longer responding to chemotherapy, SIR-Spheres microspheres have also been used successfully to shrink these tumours and extend patients' survival. There are many publications in the scientific literature on the use of SIR-Spheres microspheres in the treatment of patients with liver metastases or with primary liver cancer.[1]



Shrinkage of tumours after 6 months

WHAT WILL HAPPEN AFTER I HAVE RECEIVED SIRT?

Immediately following SIRT procedure, you may be taken for a scan to confirm that the SIR-Spheres microspheres have been infused into your liver. You will also be monitored for a few hours after the procedure to enable the treatment team to determine whether you have any side effects or complications that require additional medication.

Since you will have received a radioactive treatment, there are some simple precautions that need to be taken during the first 24 hours following SIRT procedure. The precautions include: thorough washing of your hands after going to the toilet; cleaning up any spills of body fluids such as blood, urine, or stools and disposing of them in the toilet. You will be provided with further information on these precautions by your treatment team. Your treatment team will also monitor your progress using blood tests and radiography scans at periodic intervals.

HOW SOON CAN I GO HOME AFTER SIRT?

This depends upon local hospital regulations. Normally, you can be discharged 4-6 hours after the procedure. Most patients can resume their normal daily activities two to three days after the treatment. In rare instances, some patients may need to stay overnight in the hospital for observation.

WHAT SIDE EFFECTS ARE ASSOCIATED WITH SIR-SPHERES MICROSPHERES?

Almost all treatments and drugs can produce unwanted side effects. Some side effects can be minor, making you feel uncomfortable, but a small number can be serious. Everyone is different in how he or she reacts to a treatment.

Many patients experience abdominal pain and/or nausea which normally subside after a short time and/or with routine medication. Many patients also develop a mild fever that may last for up to a week and fatigue which may last for several weeks. As a precaution, you may receive additional medications such as pain-killers, anti-inflammatory, anti-nausea and anti-ulcer drugs with your treatment with the aim of preventing or minimising these side effects.

WHAT ARE THE POTIENTIAL COMPLICATIONS FROM SIR-SPHERES MICROSPHERES?

In rare instances and even in experienced hands, there is the possibility that a small number of microspheres may inadvertently reach other organs in the body, such as the gall bladder, stomach, intestine or pancreas. If SIR-Spheres microspheres reach these organs, they may cause inflammation of the gall bladder (cholecystitis), stomach (gastritis) or intestine (duodenitis). These complications are rare, but if one of these occurs, they normally require additional

treatment. Your treatment team will have received special training to minimise these risks and to prevent them from happening.

WILL I LOSE MY HAIR?

Hair loss (alopecia) has never been reported following treatment with SIR-Spheres microspheres. If you are receiving chemotherapy this may cause hair loss, however SIR-Spheres microspheres will not make this worse.

IS THERE ANYTHING I MUST AVOID?

You *must not* receive SIRT treatment if you are pregnant and you *must not* become pregnant within two months of being treated as this may cause irreversible harm to the unborn baby. Effective contraception must therefore be used at all times during this period. You *must not* breastfeed during the first two weeks after treatment and *must not* use any milk expressed during this period for bottle feeding of your baby.

WILL I HAVE TO CHANGE WHAT I EAT OR DRINK?

No. You can and should continue to eat and drink as normal. Adequate levels of food and in particular, fluids will help you return to your normal daily activities. Your doctor is the best person to advise you regarding alcohol consumption.

Sirtex is committed to the development of innovation therapies for liver cancer in order to improve patient survival and quality of life.

For more information about Sirtex or to contact us:

SIRTeX

Sirtex Medical Limited
Level 33, 101 Miller Street
North Sydney, NSW 2060,
Australia
Tel: +61 2 9964 8400
Fax: +61 2 9964 8410

Sirtex Medical Singapore Pte Ltd
50 Science Park Road
#01-01 The Kendall
Science Park II
Singapore 117406
Tel: +65 6308 8370
Fax: +65 6778 9424

1. Data on file

545-A-0612

Frequently Asked Questions

What is Selective Internal Radiation Therapy (SIRT)?

Selective Internal Radiation Therapy or SIRT, also known as radioembolisation, is an innovative therapy that has been developed for the treatment of unresectable primary and secondary liver cancer. The technique involves infusing millions of radioactive beads (Yttrium-90 resin microspheres or SIR-Spheres® Y-90 resin microspheres) into the arterial blood supply of the liver.

What are SIR-Spheres Y-90 resin microspheres?

SIR-Spheres Y-90 resin microspheres are radioactive microspheres used in SIRT. SIR-Spheres Y-90 resin microspheres deliver targeted internal radiation therapy directly to the tumour(s) with a dose of internal radiation up to 40 times higher than conventional radiotherapy, while sparing healthy tissue.

Direct delivery of the microspheres via the hepatic arteries helps to achieve maximum disease control through optimal tumour coverage. Randomised controlled studies in patients with liver metastases from colorectal cancer have demonstrated that SIRT using SIR-Spheres Y-90 resin microspheres significantly increases the tumour response or disease control rates, as well as significantly extending the time to progression and overall survival. SIR-Spheres Y-90 resin microspheres may also reduce the size of previously inoperable liver tumours to the extent that they are amenable to potentially curative resection or ablation.

How do SIR-Spheres Y-90 resin microspheres work?

The SIRT procedure enables radiation to be targeted directly into the liver tumours by using the tumour's own blood supply. Healthy liver tissue derives up to 90% of its blood supply from the portal vein (the vein that delivers nutrients to the liver from the gut), with only a small amount of the blood supply being derived from the hepatic artery. In contrast, liver tumours derive up to 90% of their blood supply from the hepatic artery, since they need a profuse supply of highly oxygenated blood. The hepatic artery therefore provides an ideal route to deliver targeted treatment to the tumour.

SIR-Spheres Y-90 resin microspheres are between 20-60 microns in diameter which means that following infusion, they are small enough to become lodged in the arterioles within the growing rim of the tumour(s) where they emit a high dose of radiation, but are too large to pass through the capillaries and into the venous system. As SIR-Spheres Y-90 resin microspheres are targeted directly at the liver tumours via the hepatic artery, exposure to the remaining healthy liver tissue is minimised. The resin microspheres contain the radioactive element Yttrium-90, which delivers beta radiation over a relatively short distance: an average of 2.5 mm in human tissue and a maximum of 11 mm. Yttrium-90 has a half-life of approximately two-and-a-half days (64.1 hours), therefore most of the radiation (over 97%) is delivered to the tumour in the first two weeks after treatment.

How are SIR-Spheres Y-90 resin microspheres different from conventional radiotherapy?

Radiation is an effective agent for destroying tumours and is widely used in cancer treatment. However, the use of external beam radiation to treat liver tumours is limited by the low radiation doses that can be applied to the liver without the risk of radiation damage to the normal liver tissue.

Unlike conventional external beam radiation, SIR-Spheres Y-90 resin microspheres selectively irradiate liver tumours and therefore have the ability to deliver more potent doses of radiation directly to the cancer cells over a longer period of time. The therapeutic ratio with SIRT, compared to external beam radiotherapy, is significantly improved and the tumour-absorbed doses from SIRT are typically 4 to 6 times higher than those to the healthy liver tissue.

How is SIRT administered?

After a local anaesthetic is administered to the patient, the SIRT-trained interventional radiologist makes a small incision, usually into the femoral artery near the groin. A catheter is then guided through the artery into the liver. SIR-Spheres Y-90 resin microspheres are administered through this catheter. The whole procedure may take around 60-90 minutes. After the procedure is completed, patients may be sent to have a scan to check the level of

radioactivity of the SIR-Spheres Y-90 resin microspheres in the liver. Patients will be monitored for a few hours after the procedure and most patients are discharged within 24 hours.

What are the side effects of SIRT?

Almost all treatments and drugs produce unwanted side effects. Most side effects following a SIRT procedure are minor, but a small number can be serious. Many patients experience abdominal pain or tightness in their abdomen, nausea and loss of appetite which normally subsides within a week. Patients may also develop a mild fever that may last for up to a week and fatigue which may last for several weeks.

What are the potential complications of SIRT?

In rare instances, a small number of microspheres may inadvertently reach other organs in the body, such as the gallbladder, stomach, intestine, or pancreas. If microspheres reach these organs, they can cause inflammation or ulceration. These complications are rare, but if they do occur they will require additional medical treatment.

Do patients have to take special precautions?

There are some simple precautions that patients need to take during the first 24 hours following the SIRT procedure. These precautions include: thorough hand washing after using the toilet, and cleaning up any spills of body fluids such as blood, urine or stools and disposing of them in the toilet. Otherwise, patients can resume normal contact with family members.

Patients must not receive SIRT treatment if they are pregnant, and must not become pregnant within two months of receiving the treatment as this may cause harm to the unborn baby.

What is the regulatory status of SIR-Spheres Y-90 resin microspheres?

SIR-Spheres Y-90 resin microspheres are classified as a Medical Device and approved for use in for the treatment of unresectable liver tumours in Australia and New Zealand, the European Union (CE Mark), Switzerland, Turkey, and many countries in Asia such as India, Korea, Singapore, Malaysia, Thailand, Vietnam, Philippines and Hong Kong.

SIR-Spheres Y-90 resin microspheres are also full PMA-approved by the FDA and are indicated in the U.S. for the treatment of non-resectable metastatic liver tumours from primary colorectal cancer in combination with intra-hepatic artery chemotherapy using floxuridine. They are also approved in Taiwan in chemotherapy refractory metastatic colorectal cancer patients.