Brachytherapy/Protocol-Specific Procedure

Y-90 MicroSpheres (SIRSpheres®) for treatment of hepatocellular carcinoma

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Brachytherapy Device :	Y-90 SIRSpheres®
	Y-90 SIRSpheres® is a radioactive implant in the form of resin microspheres. The intended use of these microspheres is for implant into hepatic metastases from colorectal cancer via catheter placed in the hepatic artery, distributing non-uniformly throughout the liver. The microspheres are labeled with yttrium 90 (Y-90); a beta-emitting isotope that delivers the tumoricidal doses of radiation to the tumor.
Device Information Source:	Y-90 SIRSpheres® is indicated for the treatment of unresectable colorectal carcinoma metatstases to the liver. For additional information regarding this agent, consult package insert or other standard references
Applicability of Worksheet:	Clinical use of commercial product; standard of care
Target Patient Process:	Candidates for this procedure are patients who have unresectable colorectal carcinoma metatstases to the liver. Patients will be evaluated by Oncology, Radiation Oncology and Interventional Radiology (IR) staff prior to the procedure.
Administration/Treatment Schedule:	A patient is identified as a possible candidate through Oncology. This patient is referred to IR for a consult to determine eligibility. A triphasic abdomen CT and lab tests are run. In addition, a 99m-Tc MAA scan is scheduled within 1 month before a therapy through nuclear medicine to determine the extent of pulmonary shunting. The Nuclear Medicine physician calculates the pulmonary shunt and the IR physician calculates the liver mass volume to be treated. These values are supplied to the Radiation Oncologist by the IR NP assigned to the case. The Radiation Oncologist completes the Y-90 SIRSpheres® Written Directive. Details are given in the attached Protocol.
Dose Range:	A Y-90 SIRSpheres® treatment is intended to expose the liver to 80 to 150 Gy. The IR physician and Radiation Oncologist prescribe the amount of Y-90 SIRSpheres® using the Y-90 SIRSpheres® Written Directive. This dose will be verified by Medical Physics.
Necessary Training:	Initial training of a treatment team is provided by the manufacturer. Subsequent training from trained personnel is acceptable.
Scheduling Procedures:	Scheduling is coordinated through the assigned IR Nurse Practitioner. Details are given in the attached Protocol.
Written Directive and Validation:	The Radiation Oncologist will forward the written directive (Y-90 Labeled SIRSpheres® Written Directive) to medical physics after validating the dosage with the IR staff. Medical physics will FAX the written directive to the nuclear pharmacy when the dose verification is complete. Doses cannot be ordered until this form is received by the nuclear pharmacy. The original of the form will be kept in Radiation Oncology with a copy of the completed form in the Nuclear Pharmacy.
Y-90 Procurement/Preparation:	Y-90 SIRSpheres comes as a bulk vial that must be dispensed according to the written directive from the oncologist. Because it is a bulk vial and not a unit dose, inventory can be ordered before the written directive is received.

Upon notification of a pending procedure from IR via e-mail, the nuclear pharmacist fill out a Y-90 SIRSpheres order form (located at J:\Nuclear\NUCLEAR PHARMACY\Standard Operating Procedures\Therapies\Y-90 MicroSpheres – SirSpheres). The order sheet is faxed to Sirtex as directed on the order form. A confirmation will be faxed to the radiopharmacist upon verification of the availability of the dose (usually 24 hours). After ordering, a Radiopharmaceutical Requisition Form is completed, the dose is entered as inventory in the pharmacy computer system, and a notation is written on the nuclear medicine inventory blackboard. The cutoff time for ordering is by 11:00 CST on Tuesday, the week before the scheduled therapy. However, extra material is usually on hand to accommodate last minute requests, so call Sirtex to verify availability.

The SIRSpheres® package should arrive at the Nuclear Pharmacy via courier the day of the scheduled therapy. If the dose is late (after 09:30 CST), the Nuclear Pharmacist will contact SIRTex via the telephone number provided on the returned confirmation forms. The nuclear Pharmacist will also notify the nurse practitioner involved in the case.

Details for the preparation are given in the attached Protocol.

Pharmacy Product Validation: Upon delivery and check-in of product, the nuclear pharmacy will prepare the administration apparatus and will fill and dispense the prescribed dose following the SIRSpheres Preparation Procedure (Attachment 8).

Upon completion of the procedure, the radionuclide vial, tubing and any other articles contaminated with radioactive materials will be returned to the nuclear pharmacy by the Nuclear Pharmacist, and the residual activity in the delivery vial measured in a dose calibrator.

Patient Instructions/Education Validation: Patient instructions/Education validation done by the IR nurse practitioner assigned to the patient.

Administration Validation: Only appropriately trained individuals may administer this product. The source infusion is by IR staff physician, with help from medical physics. The delivered activity is determined by the Nuclear Pharmacist.

Other information/instructions: See attached SIRSpheres Protocol which includes 8 attachments.

REVIEWED BY:

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Scott Knishka, Nuclear Pharmacy

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SIR-Spheres Technical Protocol
Interventional Radiology Suite

Including _ Attachments

July 2007

Candidates for this procedure are patients who have colon cancer with liver predominant metastasis. They will be evaluated by Oncology and Interventional Radiology staff prior to the procedure.

ROOM PREP

-Put an egg crate on the table
-Load the injector with 350 Omnipaque **(NEVER VISIPAQUE IT WILL RESULT IN POOR SUSPENSION OF THE SPHERES)**
-Set up basic tray with regular flush system (3cc heparin) and regular saline in bowl

ADD TO THE TRAY:

- 1 pkg steri-strips
  - (4) 20cc syringes
  - 2 extra yellow syringes (back room of neuro)
- 1 sterile chux
- 1 sterile sheet
  - 1 low pressure tubing
  - 3 way stopcock
  - 1 extra chloraprep stick
  - Regular extra's used for an angiogram set up

-Draw up sterile water in the (4) 20cc syringes
-Draw up the 4 (yellow) 10cc syringes with contrast (350 Omnipaque **NEVER VISIPAQUE**)
-Shave and prep the groin just as you would a normal angiogram
-Place a barrier supplied by Nuclear Medicine on the floor on the side of the patient where our MD's will be standing and tape it in place

***THE TECHS AND NURSES IN THE ROOM MUST IDENTIFY THE PATIENT WHEN HE/SHE ENTERS THE ROOM BY NAME & BIRTHDATE**

ALL EMPLOYEES MUST WEAR THEIR DOSIMETER IN THE ROOM

PROCEDURE

*We will start with a diagnostic angiogram if needed (power injector)

*Next they will select the Rt. or Lt. Proper Hepatic**.** MD may need a Renegade, Tracker or similar catheter to get into the Proper Hepatic depending on the patient's anatomy.

*Next, the spheres are brought into the room. Nuclear medicine will have the spheres loaded into the Delivery Box and will deliver the spheres to the angio suite when notified by us.

***Once the spheres are brought into the room everyone is required to have on hat, mask, goggles and double gloves and no one is allowed to leave until Medical Physics monitors them for radiation**.

*Ideally there will be one Angio Tech in the room and the other outside the room. The Tech outside the room will stay outside and monitor people coming in and out of the room and get any unexpected supplies that may be needed in the room.

*Next either the Radiologist or Tech will :

-Put the small table/mayo stand along side the patient

-Put a sterile sheet on the small table/mayo stand

-Cover that sheet with a sterile chux

-The "Delivery Box" (which is not sterile) will be set on top of the sterile chux.

*The Nuclear Pharmacist will have a 3 way stopcock attached to the "B" tubing (the Radiologist may or may not add the low pressure tubing for an extension on that "B" tubing)

*Then the Radiologist will connect the contrast and sterile water syringe to the 3 way stopcock attached to the "B" tubing **(flushing will always be with sterile water NOT saline!)**

*Next the Radiologist will clean the "A" tubing coming from the "box" and connect our catheter to it. (the "A" tubing has already been primed with sterile water)

*The Interventional Radiologist will begin to inject the spheres 5cc's at a time. After each 5cc's they will flush with sterile water, inject some contrast, flush again, and continue with 5 more cc's. They will continue this until the spheres vial is empty (total of 20cc). The last step will be a contrast run to assess the vessels after all 20cc's are in (a hand run the same as the others). This process of injecting should take around 15 minutes. They do not want to inject too fast or there is potential for backflow into the bowel, This could cause many problems for the patient including potential reflux into the stomach which could cause gastritis among other problems.

*The radiologist will disconnect the catheter from line "A". The catheter will then be removed from the groin. All catheter(s) and syringes used for the infusion will be surveyed and disposed of by Nuclear Medicine.

* The radiologist will hold pressure as normal on the groin until hemostasis is achieved.

CLEAN UP AND MONITORING

*Before the patient leaves the room he/she will be checked for radiation levels in the abdominal area by the medical physicist.

*NO ONE WHO IS PRESENT IN THE ROOM WHILE THE SPHERES ARE PRESENT WILL BE ALLOWED TO LEAVE UNTIL A MEDICAL PHYSICIST HAS MONITORED THEM FOR RADIATION.

Nuclear Medicine staff will take any materials with them that have spill on them and any materials, gauze and towels, etc. that have blood or any liquid on them.

*Medical Physics staff will test all materials for residue as well as the entire room.

*NUCLEAR MEDICINE STAFF WILL PROVIDE A BIN FOR POTENTIAL RADIOACTIVE MATERIALS. Medical physicist will bring bin back to Nuclear Medicine after final room survey has been completed.

*The only time during this procedure that there is a great risk for exposure is if there is a spill. A spill should not happen as long as all people involved are careful and can focus their full attention on what is being injected without being disrupted.

*If there is a spill the main thing to do is put a barrier on top of it. **Throw a moistened chux over it, absorbent side down**. Medical Physics will determine what to do from that point. If these spheres dry they can aerosolize and possibly be inhaled.

EMERGENCIES OR CODES

* If there is a code or emergency situation, Nuclear Medicine will wrap the box up in the chux and sheet and remove it from the table. Try to keep the number of people coming in for the code to a minimum. (If you can) During and after the code **NO ONE LEAVES THE ROOM WITHOUT BEING TESTED!**

OF NOTE

Others present in the room in addition to IVR staff will include:

- Medical Physicist, who is there to monitor the room and to be available to contact the Radiation Oncologist if dose adjustments need to be made.
- Radiation Oncologist, who most often will not be present during the procedure, and is responsible for determining the dose of the spheres and for designating who the "injecting" MD will be.
- Nuclear Pharmacist who will manage the radiopharmaceutical and waste.

There will be a lot of people in the room, which makes it very important for everyone to do their job, keep noise levels down, and focus on what is happening in **THIS ROOM** with **THIS PATIENT.**

After the room survey has been completed, IVR staff are free to prepare the room for the next patient.

The patient will be transferred to a recovery area immediately following the procedure. No special precautions are necessary with regard to patient transport.

ATTACHMENTS:

1. SIRSpheres Protocol for Nuclear Medicine Staff
2. SIRSpheres Process Summary
3. SIRSpheres Statement of Responsibilities
4. List of components for emergency spill containment kit that will be present during administration.
5. SIRTex Package Insert for the Delivery Apparatus
6. Nuclear Pharmacy SIRSphere Worksheet
7. Y-90 Labeled SIRSpheres Treatment Record

Attachment 1: SIR-Spheres® Protocol for Nuclear Medicine Staff

1. **Upon receiving a written directive from the Radiation Oncologist, the nuclear pharmacist will verify that the SIR-Spheres® dose is appropriate for the patient based on the ^{99m}Tc-MAA scan and dose calculation.**

2. **The nuclear pharmacist will prepare the SIR-Spheres® dose and assemble the SIR-Spheres® Lucite delivery box as follows:**

    a) Place shipped vial of SIR-Spheres® in dose calibrator and determine the calibration factor needed to obtain the activity specified on the shipping label. Assay and record the activity of the SIR-Spheres®.
    b) Using aseptic technique in the Laminar flow hood, withdraw patient specific dose from the SIR-Spheres® shipping vial. The patient specific dose is the amount of activity on written directive + 10% extra (to account for residual losses). Place dose into the V-Vial provided by SIRTeX Medical Inc. Place the V-Vial in Lucite Vial Holder.
    c) After removing the dose, re-assay shipping vial of SIR-Spheres® in dose calibrator using the calibration factor obtained in a) and record the activity.
    d) Calculate and record activity of patient specific dose in V-Vial:

Activity recorded in a) – Activity recorded in c) = Activity of Patient dose in V-Vial

    e) Enter the calculated activity of the dose into the computer database; print labels and prescription. Label the Lucite Vial Holder.
    f) In the Laminar flow hood, place the Lucite Vial Holder (containing the V-Vial) inside SIR-Spheres® Lucite delivery box. Attach administration lines to the Lucite delivery box per SIRTeX Medical Inc. Assembly Instructions, including two 20 mL syringes with water for injection.

Note: Two 3-Way Stopcocks and a Millipore filter will be added to the administration lines.

    g) Prime the administration lines using one of the 20 mL syringes with water for injection.
    h) Insert the administration line needles into the V-Vial per SIRTeX Medical Inc. Instructions.

Note: The **medical physicist or a second nuclear pharmacist** will verify the residual activity in the shipping vial.

3. Place prepared SIR-Spheres® Lucite delivery box (containing the patient specific dose of SIR-Spheres®) on a cart and cover with single-use sterile drape. Transport to DVI procedure room.

4. Provide (and transport to DVI procedure room) a Spill Box containing the proper materials needed to contain and remove any spilled SIR-Spheres®. (See attached page for Spill Box contents)

5. Provide (and transport to DVI procedure room) an Acrylic Beta Shield Waste Container for all surgical instruments, sterile drapes, administration lines, catheters, gloves, booties, SIR-Spheres® Lucite delivery box, empty V-Vial, and any other items used during the procedure that may be contaminated with radioactivity.

6. Provide (and transport to DVI procedure room) a pancake probe (Ludlum Measurements Inc. model # 44-9) with survey meter (Ludlum Measurements Inc. model # 2241).

7. During the administration of the SIR-Spheres®, the nuclear pharmacist will:

    a) Observe the administration procedure for possible radioactive contamination.
    b) Be available with survey meter and Spill Box to contain and remove any spilled SIR-Spheres®.

8. Following the administration of the SIR-Spheres®, the nuclear medicine staff will:
    a) Assist the medical physicists (as needed) in surveying all personnel leaving the procedure room after the SIR-Spheres® have been administered.
    b) Collect all items used during the procedure that may be contaminated with radioactivity (listed in 4.) and place in the Acrylic Beta Shield Waste Container. Transport the Acrylic Beta Shield Waste Container back to the radiopharmacy after the room and personnel survey is complete.

9. Upon returning to the radiopharmacy, the nuclear medicine staff will:
    a) Survey all waste in the Acrylic Beta Shield Waste Container using pancake probe (Ludlum Measurements Inc. model # 44-9) with survey meter (Ludlum Measurements Inc. model # 2241). Properly dispose the waste per amount of contamination.
    b) Survey SIR-Spheres® Lucite delivery box and store properly per amount of contamination.
    c) Survey and properly dispose of syringes per amount of contamination.
    d) Assay V-Vial, administration lines, and catheter in dose calibrator. Record amount of radioactivity in each and determine the % residual. Using the % residual, calculate the actual activity of SIR-Spheres® administered to the patient. Record this information for the medical physics personnel.
    e) Properly dispose of V-Vial, administration lines, and catheter (after assaying) per amount of contamination.

Attachment 2: SIRSpheres Process Summary

	Steps	*Process*	***Department(s)***	***Staff responsible***
1	**Initial Evaluation by GI Oncology staff**	▪ Clinic visit ▪ Review history ▪ Determine if patient meets criteria for SIR-spheres	GI Oncology staff	Oncologist Rosemary Neider, NP
2	**Consultation with IVR Service**	▪ IVR staff review CT/PET (extent of liver involvement, portal vein patency, etc) ▪ Determine if additional scans needed ▪ Focused H&P (any contraindications to SIR-spheres; angiography; liver/renal status)	IVR staff	John McDermott, MD Myron Wojtowycz, MD Foluke Otitoju, MD Russel Paul, MD LuAnn Greiner, NP Lisa Semmann, NP
3	**Patient notification**	▪ Patient notified that he/she is candidate ▪ Patient contacted to review procedure schedule, provide patient/family education	GI Oncology staff IVR staff	All IVR NP's with MD follow-up as needed
4	**Prior Authorization**	▪ Oncology staff document clinical indication for SIR-spheres ▪ Order entry for pre-procedure exams through A2K triggers prior authorization process ▪ Onc MDs contacted by precertification nurses if additional information needed	GI Oncology staff GI Oncology/IVR staff Pre-cert Nurses	All Shannon Peterson Erin (Onc) Michelle Schwanbeck (Onc)
5	**Pre-procedure radiological exams**	**Hepatic artery angiogram** ▪ To evaluate hepatic arterial anatomy **Nuclear Medicine liver/lung scan** ▪ To evaluate % of lung shunting	IVR staff Nuclear medicine staff	All All
6	**Final determination that patient is a candidate**	▪ **No contraindications on clinical exam** ▪ No contraindications on hepatic angiogram ▪ Less than 20% lung shunting	GI Oncology & IVR staff	Consulting MDs
	Rad Onc Consult	▪ **Consult/Eval by Radiation Oncology**	Rad Onc Staff	Kristin Bradley, MD Mark Ritter, MD Rakeh Patel. MD Steven Howard, MD
7	**Determine dose**	▪ **Review CT scan to determine tumor-to-liver volume** ▪ **Prescribe SIR-spheres dose**	IVR & Rad Onc Rad Onc MD	IVR staff & Radiation Oncologist Radiation Oncologist
8	**Schedule SIRT procedure**	▪ **Coordinate procedure date with IVR, Nuclear Medicine, and Radiation Oncology staff** ▪ **Order entry through A2K**	IVR MD staff Nuc Med Radiation Oncology IVR staff	Consulting MD Nuclear Pharmacist Radiation Oncologist Bruce Thomadsen, PhD Shannon Peterson
		▪ **Contact patient (review procedure prep)** ▪ Reserve pre/post procedure care ▪ Arrange overnight housing	IVR staff	LuAnn Greiner, NP Lisa Semmann, NP
9	**Order spheres**	▪ **Order at least 1 week in advance of SIRT**	Nuclear Medicine	Nuclear Pharmacist
10	**Prepare spheres**	▪ **Prepare the treatment device and dose** ▪ Verify activity in treatment vial	Nuc Med Radiation Oncology	Nuclear Pharmacist Medical Physicist
11	**Perform SIRT**	▪ **Patient arrives APC for procedure prep** ▪ Verification of patient identity (name & DOB) ▪ Procedure performed in IVR suite ▪ Patient/room survey post procedure ▪ Post procedure care in APC or inpatient unit (*under IVR or Onc Service)*	IVR Nuclear Medicine Radiation Oncology staff	IVR (MDs, RN, 2 Techs) Nuc Med (RPh) Medical Physicist

Attachment 3: SIRSpheres: Statement of responsibilities

1. Admission (when indicated) will be on B6/6 on the Medical Oncology Service. If a > 24 hour stay is anticipated the patient will be admitted to F6/6.
   Nuclear Medicine will complete the PSN on-line Occurrence Screen

2. Interventional Radiology will:
   - Consult the patient, performing a history and physical, and a review of the procedure with the patient before scheduling the screening examinations (MAA scan and angiogram).
   - Inject the microspheres under the authority of Radiation Oncology.
   - Do further follow-up and take care of post embolization problems in conjunction with Medical Oncology. The Nurse Practitioner in Interventional Radiology will coordinate further follow-up for future rounds of treatment.
   - Assume responsibility for coordination/follow-up with any future treatment rounds

3. Nuclear Medicine will perform and report on the evaluation ^{99m}Tc-MAA images.

4. Radiation Oncology will:
   - Consult the patient, evaluating the proposed treatment.
   - Write the prescription for the treatment.
   - Respond to patient problems involving radiation effects

   .
5. Medical Physics will:
   - Validate the prescription.
   - Deliver the prescription to the Nuclear Pharmacy.
   - Verify the activity in the patient –dose vial by checking the residual activity in the shipping vial.
   - Attend the treatment procedure to verify correct assembly of the treatment device.
   - Measure the exposure rates around the patient following infusion of the microspheres and check the personnel and area for contamination.
   - Determine the compliance of the treatment with the prescription.

6. Nuclear Medicine Pharmacy will:
   - Order the prescribed activity of microspheres.
   - Receive, log in, and assay the microspheres when they arrive.
   - Prepare the dose and delivery apparatus, and primed with sterile water.
   - Manage the disposal of the radioactive wastes.

7. The individuals present in the room should include:
   - Two IVR Technologists (1 in and 1 out)
   - Interventional Radiologist
   - Nuclear Pharmacist
   - Medical Physicist

Attachment 4: List of components for emergency spill containment kit that will be present during administration.

General Box (Box 1)

Item	Purpose
Radiation Monitor	Check surfaces, equipment and personnel for possible contamination
Disposable Materials	
• Plastic bags	Receive waste
Absorbent Plastic Backed Pads (Low Shedding)	Place under all equipment or containers to contain any spills
• Paper hand towels	General use
• Disposable cups with lids	Received used materials during the procedure; transfer to appropriate containers after stock-take
• Gauze swabs	General use
• Sterile disposable gloves	General use
Trefoil Tape and Pens	Labelling containers with contaminated materials (tape) and for labelling disposables and recoverables containers.
Containers to Collect Waste	
• Baskets	Lined with plastic bags for collection of all used items except instruments and sharps. Generally have two, one for disposables, one for recoverables
• Rigid containers	For collection of sharps and instruments. Generally have a dedicated sharps container and another for recoverable instruments
Disposable Plastic Sheet	Place on the floor under the trolley with the delivery apparatus on it. Allows rapid and safe removal of any spill on the floor during the procedure
Decon 1:10 Dilution	General cleaner for wiping surfaces during room clearance and cleaning surgical instruments during the procedure

Spill Pack (Box 2)

Item	Purpose
Disposable Materials	
• Plastic bags	Receive waste
• Absorbent plastic backed pads (Low Shedding)	Place over spills for rapid containment and assistance in removal
• Paper hand towels	General use
• Plastic overshoes	Reduce spread of contamination and protection for staff dealing with the spill
• Plastic apron	Reduce spread of contamination and protection for staff dealing with the spill
• Disposable gloves	General use
Trefoil Tape and Pens	Labelling containers with contaminated materials
Surgical Gown	Staff protection
Decon Concentrate (10%)	Remove all spilled material from surfaces.

Attachment 5: SIRTex Package Insert for the Delivery Apparatus

SIRTeX Medical Inc

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270 E Westminster
Lake Forest IL 60045 USA
Tel: + 1 847 482 9023
Fax: + 1 847 234 2115
Email: sirtex@sirtex.com
Made in Australia

DAL-US

SIR-SPHERES® DELIVERY APPARATUS

INSTRUCTIONS FOR USE

READ THE FOLLOWING INSTRUCTIONS BEFORE IMPLANTING SIR-SPHERES®

Introduction

The information and steps described below are the recommended procedures for the use of the Delivery Box, Delivery Set and V-Vial.

The perspex Delivery Box with the V-Vial holder acts to shield the operating room staff from beta radiation emitted by SIR-Spheres®. The Delivery Set and V-Vial are used for the delivery of SIR-Spheres®.

SIR-Spheres® can be administered via the hepatic artery by one of two routes, 1) an implanted hepatic artery port or 2) a trans-femoral catheter. If a needle is used to puncture an implanted hepatic artery port, then the internal diameter of the needle must not be less than 0.65mm (i.e. gauge 20). If a port is used to deliver the SIR-Spheres® then it is absolutely necessary to be completely sure that the catheter is placed correctly so that the SIR-Spheres® go only to the liver and not to any other organs, such as the duodenum or stomach. If a trans-femoral catheter is used then it should have as large an internal diameter as possible in order to prevent any chance of blocking. It may be preferable to use a micro-catheter but the operator must be aware that fine bore catheters may block unless the SIR-Spheres® are delivered as a very dilute suspension. *Small bore catheters and needles may block with SIR-Spheres®.*

If vasoactive agents are to be injected into the hepatic artery, they are injected prior to SIR-Spheres® through the Flushing Tube 'B' directly into the line that goes to the patient.

The Valve Control Knob on the front of the Delivery Box makes it possible to operate the 3-Way Valve of the Delivery Set without reaching into the box. The Valve Control Knob is limited to a one quarter turn when properly engaged. This limit is a safety feature designed to prevent the injection of SIR-Spheres® into the Flushing Tube.

Equipment Required

Delivery Set, Delivery Box including V-Vial Holder, V-Vial, SIR-Spheres®, two 20ml syringes filled with water for injection.

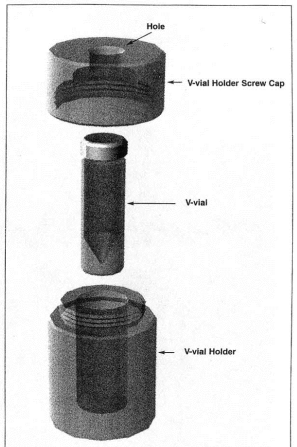


Diagram 1)

Assembly of Delivery Set in Delivery Box

1. Dispense the required patient specific dose of SIR-Spheres® from the shipping vial into the V-Vial. The volume of the patient specific dose should be 3-5mls. *If the total volume in the V-Vial is less than 3ml, add sufficient extra water for injection (NOT SALINE) to bring the volume to a minimum of approximately 3ml.*

2. Confirm that the dose of SIR-Spheres® contained in the V-Vial is correct for the patient.

3. The Medical Physics or Nuclear Medicine technician or pharmacist drawing up the patient specific radiation dose should put the V-Vial into the V-Vial Holder and replace the screw cap on the perspex V-Vial Holder.
   (See Diagram 1)

4. Remove the sterile Delivery Set
   (See Diagram 2) from the package and keep sterile. Take care not to take the shields off the two needles, as this will break sterility.

5. Firmly place the 3-Way Valve into the bracket on the back wall of Delivery Box so that tube 'A' leads up, tube 'B' leads down and tube 'C' leads to the right. **(See Diagram 3)**

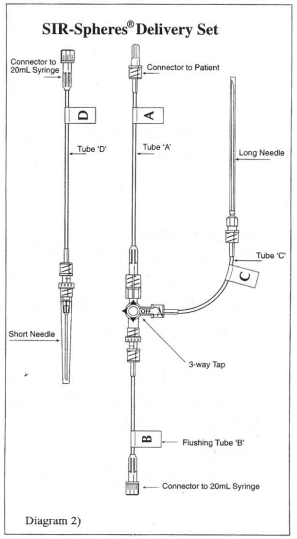
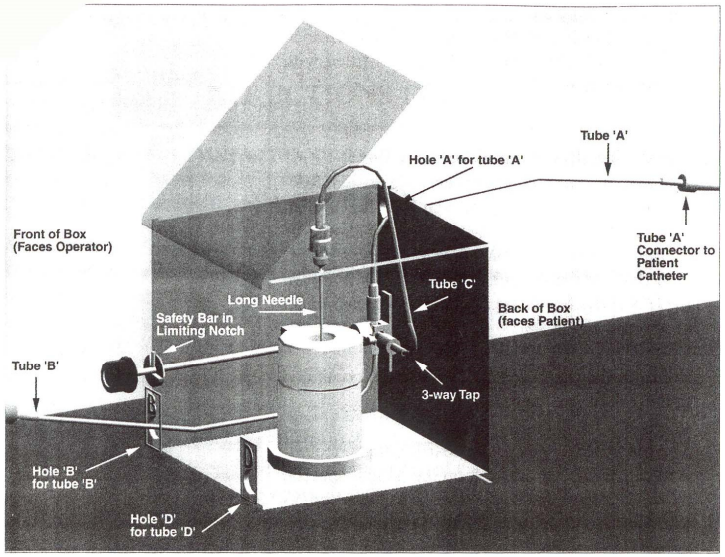


Diagram 2)



gram 3)

From inside the Delivery Box insert tubes 'A' and 'B' through the corresponding holes in the Delivery Box. The holes in the Delivery Box are color coded and marked with 'A' and 'B'. Tube 'C' with the needle attached is left in the box. **(See Diagram 3)**

From inside the Delivery Box insert tube 'D' through Hole 'D' in the Delivery Box so that the needle stays inside the Delivery Box and the tubing passes outside. **(See Diagram 4)**

Push the Valve Control Knob in so that the cupped end engages firmly onto the 3-Way Valve. Ensure that the Valve Control Knob is fully engaged to the 3-Way Tap so that it is limited to one quarter turn by the small safety bar on the outside shaft of the Valve Control Knob. This requires the safety bar on the shaft of the Valve Control Knob to be firmly seated in the limiting notch.

Remove the caps from the end of Flushing Tube 'B' and tube 'D' and attach 20ml syringes filled with water for injection (NOT SALINE) to the tubes 'B' and 'D' on the outside of the Delivery Box.

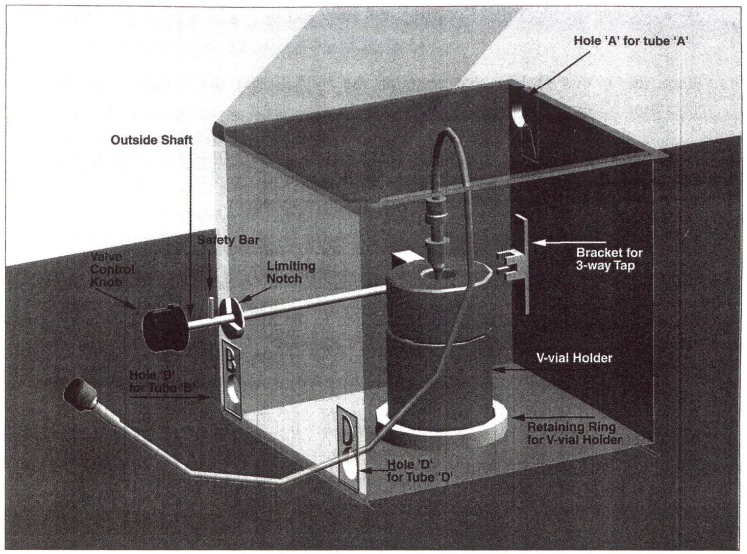


Diagram 4)

10. Prime all tubes with water for injection (see below).
This is done with covers left on needles to maintain sterility.

10.1. Note that there are one-way valves fitted to the tubes 'B' and 'D' to prevent any possibility of SIR-Spheres® being injected back into either of the syringes.

10.2. To enable flushing of all tubes with water for injection, partially disengage the Valve Control Knob to allow more than the limited one quarter turn. This requires the safety bar on the shaft of the Valve Control Knob to be just free of the limiting notch, while still being engaged enough to control the 3-way valve.

10.3. In order to prime the tube from the 3-Way Valve to the Long Needle (labeled 'C'), rotate the Valve Control Knob 90° counter clockwise (9 o'clock position) past the normal limit to allow water to flow through the 3-Way Valve into tube 'C'. *This is the only time it is recommended to disengage the Valve Control Knob by pulling it out slightly to allow full rotation.*

10.4. Re-engage the Valve Control Knob fully so that it is limited to one quarter turn.

11. Place the V-Vial Holder that contains the V-Vial with the SIR-Spheres® into the Retaining Ring in the Delivery Box.

12. Swab the V-Vial septum with alcohol. Do this by quickly removing the V-Vial holder lid, swab V-Vial septum with alcohol and then carefully replace V-Vial holder lid. Do not swab V-Vial holder with alcohol as crazing may occur.

Care must be taken when inserting needles not to contaminate them.
If contamination occurs, then discard Delivery Set and get a new one.

3. Remove cover from shorter needle (attached to the tube labeled 'D'). *This tube contains a one-way valve to prevent any SIR-Spheres® flowing back into the delivery syringe.*

4. Insert the short needle 'D' through one side of septum and push it into the V-Vial all the way up to the hub **(See Diagram 4)**. *It is important that this needle goes to the bottom of the V-Vial so that when water is injected it will swirl the SIR-Spheres® into a thin suspension. The SIR-Spheres® will be decanted from the top of the V-Vial. An excessively concentrated suspension of SIR-Spheres® may cause clogging in the fine catheter.*

5. Remove cover from Long Needle (labeled 'C').

6. Insert the Long Needle through the V-Vial septum until it penetrates approximately 10mm below the surface of the water in the V-Vial containing the SIR-Spheres®. *SIR-Spheres® delivered to the patient must be decanted from the top of the V-Vial so the suspension remains dilute and does not clog the catheter.*

7. Remove cap on tube 'A' and connect tube 'A' to the patient, either via a surgically implanted hepatic artery port, or to a trans-femoral catheter. *It is preferable not to use another 3-way tap to the patient because the SIR-Spheres® may deposit in the corners of the 3-way tap and become trapped.*

The apparatus is now ready for delivery of the SIR-Spheres® .

When the apparatus is fully assembled, injecting water from the syringe on tube 'D' will cause the SIR-Spheres® to swirl into a suspension and pass into tube 'C' and then into tube 'A' that is connected to the patient.

If using a vasoactive agent, it is injected through the Flushing Tube 'B'. To do this disconnect the 20ml syringe and connect the syringe with vasoactive agent. Ensure safety bar is at the 12 o'clock position to allow flow directly to patient, and then return safety bar to 3 o'clock position.

With the safety bar at the three o'clock position deliver slowly from the Delivery Syringe (connected to the tube labeled 'D') at a rate of approximately 5ml per minute. It is important to ***deliver slowly*** *to reduce the possibility of SIR-Spheres® refluxing back down the hepatic artery and into other organs such as the stomach or pancreas. In order to achieve a slow delivery rate and to maintain the SIR-Spheres® in suspension, the flow from the delivery syringe may be given in pulses of 0.25ml-0.5ml, separated by a pause. Use 20 mls of water for injection to deliver patient dose.*

18. At all times observe the V-Vial and tubing to ensure that the SIR-Spheres® are flowing properly and there is no leakage, blockage or air bubbles. *If the delivery of the microspheres is paused for any reason, continually flush lines with water for injection from tube 'B' to prevent microspheres in the lines from settling out and blocking. If blockage does occur, it can be cleared by flushing water with the flushing syringe.*

19. When 20mls has been delivered via tube 'D', there will still be some water and SIR-Spheres® left in the V-Vial. In order to deliver this last remaining amount out of the V-Vial, **push the long needle to the bottom of the V-Vial,** then inject air into tubing 'D' (Approx 5mls). This will cause all the remaining fluid to empty from the V-Vial.

Care must be taken to prevent air from entering the tubing going to the patient.

20. If using a transemoral catheter, the specialist should periodically stop the delivery of SIR-Spheres® and inject IV contrast through the Flushing Tube 'B' and perform fluoroscopy. This is an essential step to ensure that the catheter remains in the correct position in the hepatic artery at all times and also to ensure that no reflux is occurring back down the hepatic artery.

20.1 IT IS ABSOLUTELY ESSENTIAL TO ENSURE THAT NONE OF THE SIR-Spheres® ARE ALLOWED TO ENTER THE GASTRODUODENAL ARTERY OR OTHER SMALL ARTERIES THAT PASS FROM THE LIVER TO THE STOMACH OR DUODENUM. IF THERE IS ANY RISK OF THIS OCCURRING THEN ABANDON THE PROCEDURE.

20.2 NOTE THAT ONLY SPECIALISTS THAT HAVE RECEIVED INSTRUCTION FROM SIRTEX MEDICAL LIMITED ARE TO DELIVER SIR-Spheres®.

21. When all of the SIR-Spheres® have been delivered, the catheters are flushed and the tubing removed.

Attachment 6:
Nuclear Pharmacy
SIR-Spheres® Worksheet

Date:
Patient Name:
MR #
Requested Dose:
Dispensed Dose (110%):

Pre-procedure Readings:

Activity of Shipped SIR-Spheres®	Calibration Factor	Activity of Shipped SIR-Spheres® After Dose Withdrawn	Calculated Activity of Dispensed Dose
mCi @ CST		mCi @ CST	mCi @ CST

Post-procedure Readings:

Activity of V-vial	Activity of Administration Lines	Activity of Catheter	Calculated % Residual	Calculated Activity Patient Received	Calculated % Dose Patient Received
mCi	mCi	mCi	mCi	mCi	%

Comments: