

1. Procedure Preparation

- Notify Pharmacy procedure is starting
- Notify recovery room the procedure is starting
- Ensure CT scans are available
 - Preferably with excellent arterial phase down to groin and portal vein (PV) phase and good view of inferior vena cava (IVC) in coronal view
- Determine double balloon catheter size (available in 50 mm or 62 mm)

2. Patient Preparation: Prior to Treatment

- Blood Products (Type & Cross)
 - Packed red blood cells
 - Fresh frozen plasma
 - Platelets
 - Cryoprecipitate
- Hydration
 - Begin hydration the night prior to or day of procedure as per institutional practice
- Antibiotics
 - Consider checking recent history of hepatobiliary surgery of ablative procedures
- Allopurinol (if tumor burden >25%)
 - To prevent renal failure from tumor destruction, administer 300 mg/daily orally 2-3 days before and 2-3 days following perfusion
- Proton Pump Inhibitors
 - To prevent gastritis which may occur as a result of regional melphalan absorption during the procedure, administer proton pump inhibitors (for example: omeprazole, one 20 mg delayed release capsule by mouth) the day before and the morning of the procedure

Patients receiving angiotensin converting enzyme inhibitors or calcium channel blockers must temporarily discontinue these drugs before the procedure to prevent their interference with peri-procedural management of hypotension.

3. Procedure Room Checklist

- Power injector for Drug
 - One (1) 48" injection catheter
 - Five (5) 3-way stopcocks (PC-body, High Density Polyethylene (HDPE) or Acetal-Handles) or equivalent
 - Three (3) 20 mL syringes (PP-Barrel & Polyisoprene-Plunger) or equivalent
- Optional: Double-barrel power injector
 - For arterial DSA (digital subtraction angiography) and possible CACT (C-Arm CT)
- Catheters and wires
- Microcatheters
 - Microcatheters (Maximal Distal End OD = 2.8F) – for Selective Drug Infusion (at Interventional Radiologist discretion). Select one from Delcath qualified microcatheters listed below:
 - Merit Maestro (Merit Medical Systems, Inc., So. Jordan, UT, USA)
 - BSC Renegade Hi-Flo (Boston-Scientific Corp.; Natick, MA, USA)
 - Terumo Progreat (Terumo Medical Corp., Somerset, NJ, USA)
- Microwires
- NTG (Nitroglycerin) loaded in 10 ml syringe
- Double Balloon Catheter and Sheaths from CHEMOSAT
- Optional: Extra Items to Consider
 - 60 mL syringe x 2 for balloons
 - 20 mL syringe x 2 for contrast and NS flush
 - Extra 3-way stopcock
 - Ultrasound for vascular access
 - Embolization Equipment
 - Extra chemo disposal waste container

4. Anesthesia Patient Positioning

- Arterial line (left radial preferred)
- Foley catheter
- Triple lumen in left internal jugular vein
 - CVP, pressor, fluids
- Large bore peripheral intravenous line
- If needed, prepare for cone beam CT

5. Vascular Access

- Right IJV (Internal Jugular Vein)
 - 10F venous return sheath
- Right CFV (Common Femoral Vein)
 - 5F sheath
- 5F femoral arterial sheath

6. Arteriography and Embolization

- Superior mesenteric artery (SMA) arteriogram
- Celiac trunk arteriogram
- Common hepatic artery (CHA)
- Optional: Embolize non-target arteries if needed
- Diagnostic arterial catheter for selective catheterization

7. Anticoagulation & Insertion of Double Balloon Catheter (DBC)

- Place 18F Venous Sheath
- Inform Anesthesia
 - Give heparin 300U/kg with minimum ACT >400
 - Check every 5 min until we get to target ACT
 - Maintain every 15-30 minutes
- Introduce double balloon catheter over the wire
 - The cephalad balloon above highest hepatic vein, and the caudal balloon below the lowest hepatic vein
- Remove wire, flush catheter and saline lock

8. Connecting Catheters to Circuit

- Remove sterile wrap from venous return line and connect to stopcock of 10F RIJW sheath
 - Flush NS (normal saline) to fill line
 - Open to patient
- Perfusionist removes sterile wrap from hemofiltration circuit double balloon catheter (DBC) line
- Ensure wet connection of circuit to DBC

9. Establish Hemofiltration Circulation

- Start pump, slowly increase RPM control to achieve max allowable flow rate in the bypass circuit without flow induced vibration or exceeding the 0.80 L/min flow rate or -250 mmHg pre-pump pressure
- Keep ≤0.80L/min and no more than -250mmHg pre-pump pressure (usually 0.40-0.75 L/min)
- Pre-cartridge pressures should not exceed 200 mmHg
- Perfusionist and Anesthesiologist
 - Monitor blood flow rates
 - Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Heart Rate, vitals, ACT (activated clotting time)
 - Bubble-trap for entrapped air
 - Leaks from any part of circuit

10. Isolating the IVC

- Anticipate blood pressure drop
 - Keep Mean Arterial Pressure above 65 mmHg
- Give vasoactive agent to assess responsiveness to agent
- Max balloon volume (38 mL)
 - Do not over expand
- Push balloon into right atrium (RA) and inflate top balloon in RA, 15 - 25 mL dilute contrast (e.g. 35% dilution)
- With the caudal balloon collapsed, slowly retract the Double Balloon catheter until the cephalad balloon is at the junction of the right atrium and inferior vena cava
- If needed, further expand the cephalad balloon until indentation of the iaphragmatic hiatus is visible at the inferior margin (the balloon will acquire an acorn shaped appearance)
- Inflate lower balloon with dilute contrast medium until the lateral edges start to become effaced by IVC wall

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10. Isolating the IVC

- After balloon inflation, assess blood pressure for 2 to 5 minutes before proceeding (blood pressure could potentially drop)
- Perform DSA (digital subtraction angiography) venogram through DBC
- Reduce pump speed to 1000 RPM
- Clamp off circuit
- Inject contrast through CONTRAST port to verify balloon position.
- Unclamp circuit and return to prior RPM

Never Adjust the Position of the Double Balloon Catheter Unless Both Balloons are Fully Collapsed

- Consider marking catheter with marker at sheath level to monitor retraction back into patient
- Second operator will hold traction on DBC for rest of procedure, check position every 4-5 minutes with fluoroscopy

11. Bring Hemofiltration Cartridges Online

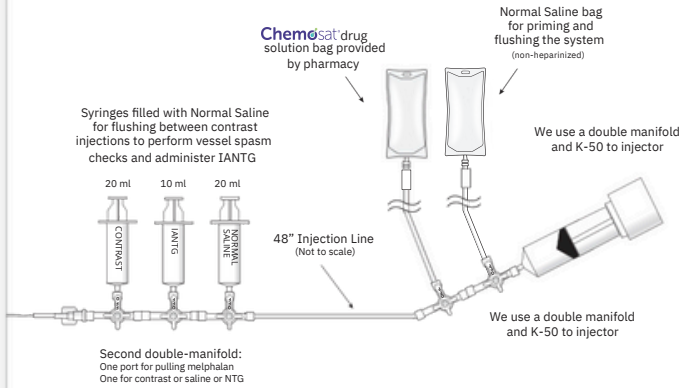
Anesthesia:

- Prepare for anticipated significant decreases in blood pressure (BP) with vasoactive agents
- Continuous monitoring and BP (blood pressure) checks

Perfusion:

- Open clamps on first filter
- Allow blood to displace heparinized NS into patient
- After first filter and its lines fully replaced with blood, wait 30 seconds and manage blood pressure, then open clamps on next filter while keeping bypass line open
- After filters and lines fully replaced with blood, wait 30 seconds while managing blood pressure, once blood pressure is stable then close bypass line
- Add redundant bypass closure clamp
- Melphalan should start within 5 minutes of bringing the filters online

12. Infusion



500 mL TOTAL INFUSION (25mL)

Close bypass line prior to infusion of drug
Minimize time between filters online and infusion



250 mL TOTAL INFUSION (25mL)

Close bypass line prior to infusion of drug
Minimize time between filters online and infusion



● MELPHALAN INFUSION ● REFILL SYRINGE. CHECK FOR BALLOON/ CATHETER PLACEMENT & SPASM



Warning: Melphalan administration should start within 30 minutes of its preparation in pharmacy and melphalan infusion should complete within 60 minutes of the start of melphalan preparation. Once filters are brought online the start of melphalan infusion should be within 5 min.

- Set up as illustration above
- Prime with normal saline, fill injector syringe with approximately 120 mL of diluted drug, purge air from system
- When the circuit is running satisfactorily and patient is hemodynamically stable, flush the hepatic arterial infusion line with normal saline to avoid directly mixing heparin with drug
- Connect drug infusion line to hepatic artery infusion catheter to complete circuit
- Confirm patency of hepatic artery
- If spasm, consider NTG
- Assess arterial patency approximately every 4-5 minutes via contrast administration during drug infusion
- Flush injection line with normal saline after contrast injections
- Ensure bypass line is closed prior to infusion of drug, minimize time between filters online and infusion.
- Infuse first dose of chemo (100 ml) at 25 mL/min
- After prescribed dose is fully administered, continue extracorporeal filtration for an additional 30 minutes (washout period)

13. Stopping Extracorporeal Circulation

- Aspirate and hand-deliver drug from system
- After washout, deflate caudal balloon fully
- Deflate cephalid balloon fully
- Discontinue filtration by:
 - Reducing the pump RPM to 1,000
 - Close circuit inflow and circuit return clamps to discontinue extracorporeal circulation
 - Stop flow by turning off the pump

14. Catheter Removal

- Remove arterial infusion catheter
 - Leave arterial sheath in until coagulation status has been normalized
- Remove DBC from sheath and replace with 18F obturator so that obturator hub bottoms out onto sheath hub (insert completely)
- Close stopcock on 10F RIJIV sheath sideport and disconnect from venous return line and flush with saline
- Do not remove vascular sheaths until coagulation status has been normalized or utilizing closure devices
- Dispose of all components appropriately in accordance with hospital, local, state, and federal biohazard guidelines

15. Normalization of Coagulation Status for Sheath Removal

- Administer protamine sulfate by slow intravenous infusion in a dose appropriate to the amount of heparin given and the activated clotting time
- Administer 10 units of cryoprecipitate and/or Fresh Frozen Plasma (FFP) based on coagulation profiles to correct remaining abnormalities, if indicated, per institutional guidelines
- Repeat coagulation profile
- Correct remaining coagulopathy following institutional guidelines. The following recommendations are provided for consideration:
- Measure blood platelet levels to determine if replacement is needed
- Follow institutional guidelines for administration of packed red blood cells for anemia
- All sheaths may be removed if the platelet count is greater than 50,000/mm³ and after the patient's coagulation status has normalized. Compress puncture sites until adequate hemostasis is achieved
- Dispose of all components appropriately in accordance with hospital, local, state, and federal biohazard guidelines
- Carefully monitor the patient until complete recovery

Coagulation Profile	Action
Prothrombin time greater than 2 seconds of normal	Administer Fresh Frozen Plasma
Partial thromboplastin time greater than 5 seconds of normal	Administer protamine