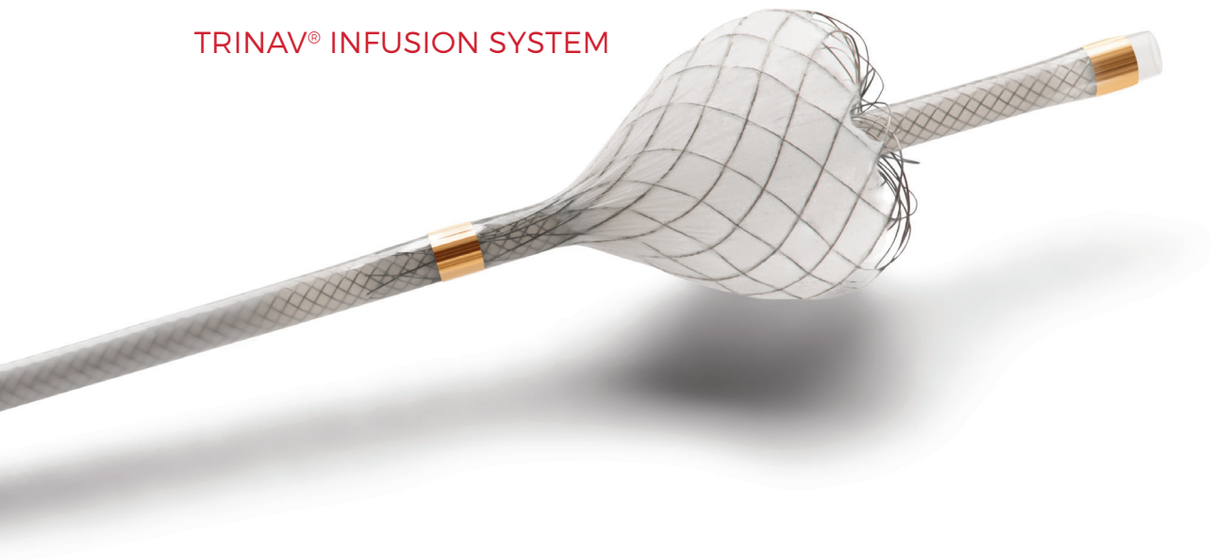
TRINAV® INFUSION SYSTEM



TriNav®
TECHNICAL USER GUIDE

The TriNav Infusion System is a 0.021-inch lumen microcatheter with SmartValve™ technology. The SmartValve self-expanding tip enables delivery of therapeutic agents to selected sites in the peripheral vascular system, including solid tumors in the liver.[1,2]

In laboratory studies, SmartValve has demonstrated the ability to generate pressure during infusion.[3] In small prospective and retrospective clinical studies, SmartValve delivered more therapy into the vasculature of liver tumors while decreasing exposure to normal tissue.[1,2]

Intended Use: The TriNav Infusion System is intended for use in angiographic procedures. It delivers radiopaque media and therapeutic agents to selected sites in the peripheral vascular system.[4]

Contraindications: TriNav is not intended for use in the vasculature of the central nervous system (including the neurovasculature) or central circulatory system (including the coronary vasculature).[4]

Precautions: Handle the device carefully. Avoid contact with sharp instruments or abrasive materials, and exposure to organic solvents (e.g. alcohol) as structural integrity and/or function of the device may be impaired.

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1 Titano et al Study Design: A retrospective, single-center study included 88 treatment-naive patients with solitary HCC tumors <6.5 cm who underwent treatment utilizing either SIS (n = 18) or standard EH microcatheters (n = 70). Twenty-three patients (5 SIS, 18 EH) received a liver transplant during the study, with 1 SIS and 6 EH patients excluded from the tumor necrosis analysis for receiving subsequent therapies prior to transplant. A pathologist performed a blinded review of the liver explant specimens to assess tumor necrosis and treatment distribution. Pathological analysis of explanted livers showed greater concentrations of microspheres within the tumor relative to the surrounding tissue in SIS explants (88.7 ± 10.6%) versus the EH explants (55.3 ± 32.7%) (p = 0.002). Titano JJ, et al. *Cardiovasc Intervent Radiol.* 2019;42:560-568.

2 Pasciak et al Study Design: A prospective study including 9 patients with unresectable liver cancer who were enrolled for the treatment of HCC (n = 6), liver-dominant metastatic disease (n = 2) or intrahepatic cholangiocarcinoma (n = 1). Each patient was treated via standard EH microcatheter or SIS. Decreases in hepatic non-target embolization were found in all patients when the microvalve catheter was used (mean 42%; σ=19%), representing a 24%–89% reduction. Increased tumor deposition was also noted in all patients (mean 68%; σ=20%), representing a relative increase of 33%–90%. Both findings were statistically significant (P<0.05). Pasciak AS, et al. *J Vasc Interv Radiol.* 2015;26:660-669.

3 Durham Study Design: This laboratory study evaluated a microvalve infusion catheter vs a standard end-hole microcatheter. A hydraulic circuit representing physiological vasculature was used to empirically investigate the ability of the microvalve infusion catheter to selectively pressurize distal vasculature using both embolic and viscus media and verify computational model predictions. The Windkessel model provides a mathematical analogue of the behavior of the system in vivo. Durham E, Jaroch D, Hunter K. Poster presented at: World Conference on Interventional Oncology (WCIO); May 6-9, 2015; New York, NY.

4 TriSalus™ TriNav™ Infusion System, Instructions for Use.

TriSalus LIFE SCIENCES®

Rx only. For the safe and proper use of the TriNav device, refer to the Instructions for Use.

TRINAV IS COMPATIBLE WITH:

- 0.035 inch wire-compatible base catheters
- Standard guide wires up to 0.018 inch
- Embolic hydrogel particles 500 µm or less and glass microspheres 110 µm or less in size
- Vessel sizes between 1.5 mm and 3.5 mm

RECOMMENDED ACCESSORIES

- 3 cc and 20 cc luer lock syringes
- Heparinized saline or equivalent flushing solution
- Tuohy-Borst adapter
- Guide wire, maximum diameter 0.018 in (0.46 mm)
- Sheath introducer (5F, 5.5F, or 6F)
- Base catheter (minimum inner diameter 0.035 in)

OPTIONAL ACCESSORY: POWER INJECTOR

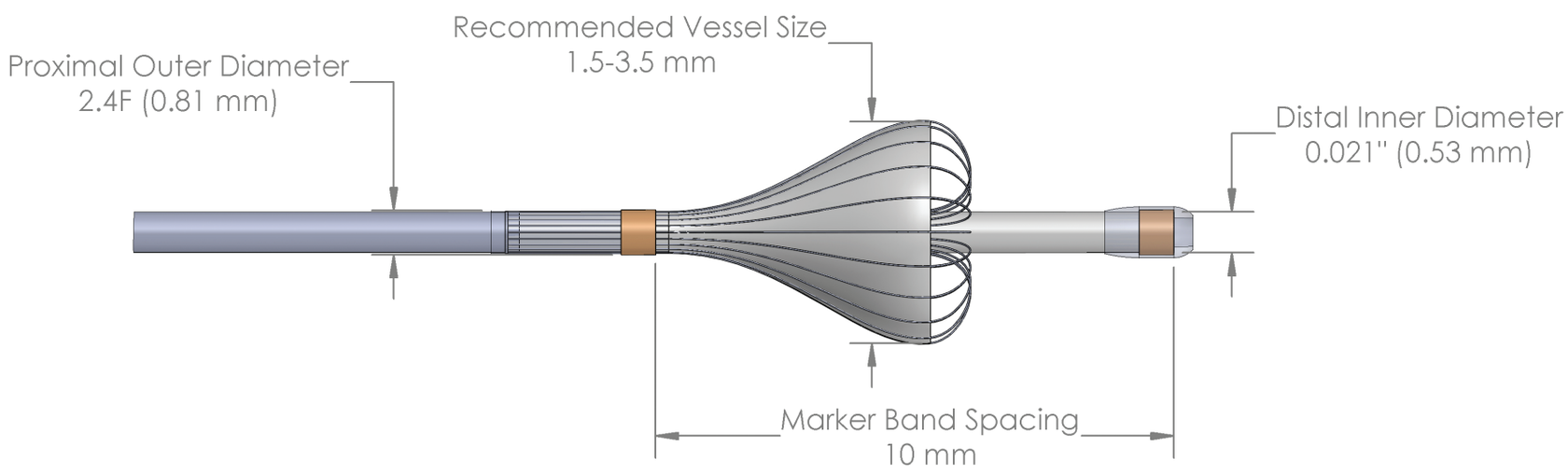
A power injector may be used to infuse contrast media through the device. The flow rate depends upon factors such as the viscosity of the contrast media, the model and setting of the power injector, and how the injector is connected to the device. The observed flow rate values indicated below are for reference only.

	Usable Length	
	120 cm	150 cm
Catheter ID	0.021”	0.021”
Dead Space Volume (mL)	0.37	0.44
Infusion Medium	Omnipaque 300 (Iodine 300 mg/mL)	Omnipaque 300 (Iodine 300 mg/mL)
Viscosity (cP)	6.3	6.3
Actual Flow Rate at 1200 psi / 8274 kPa (mL/sec)	2.6	2.1

Warning: Do not use a power injector to infuse agents other than contrast media, as the catheter may become blocked.

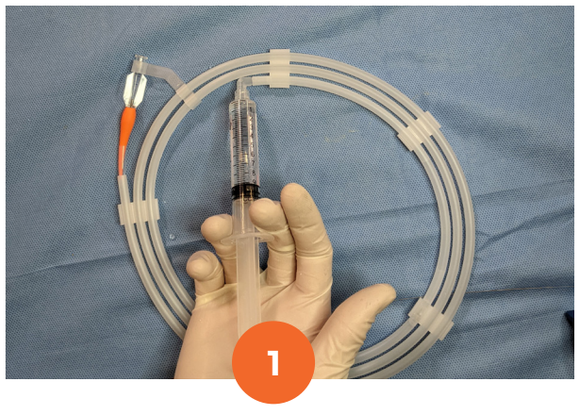
SPECIFICATIONS

Ordering Code	Inner Diameter	Vessel Size	Usable Length	Proximal Outer Diameter	Dead Space	Max Infusion Pressure	Bead Size Compatibility
120 cm CATHETERS							
TNV-21120-35	0.021 in	1.5 – 3.5 mm	120 cm	2.4 F	0.37 mL	1200 psi	Hydrogel ≤ 500 µm Glass ≤ 110 µm
150 cm CATHETERS							
TNV-21150-35	0.021 in	1.5 – 3.5 mm	150 cm	2.4 F	0.44 mL	1200 psi	Hydrogel ≤ 500 µm Glass ≤ 110 µm

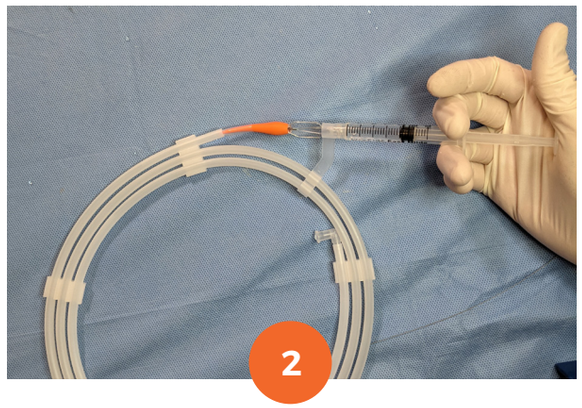


Rx only. For the safe and proper use of the TriNav device, refer to the Instructions for Use.

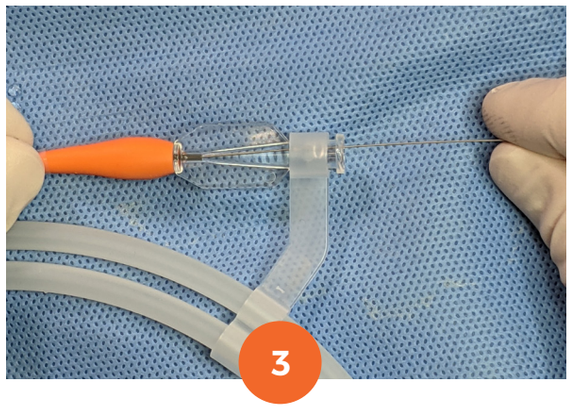
HYDRATING THE DEVICE



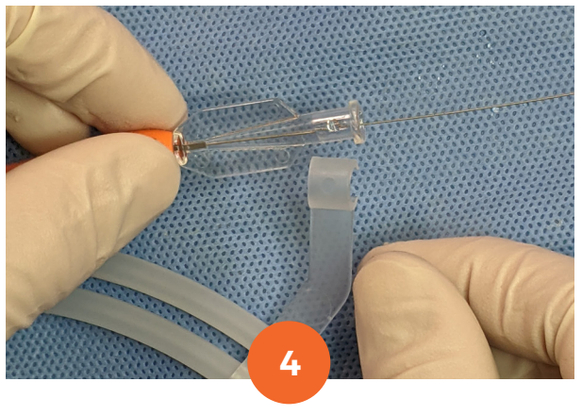
Flush the coil dispenser tube with heparinized saline to hydrate the hydrophilic coating on the outer surface of the catheter. Flush until saline can be seen exiting the tubing near the hub.



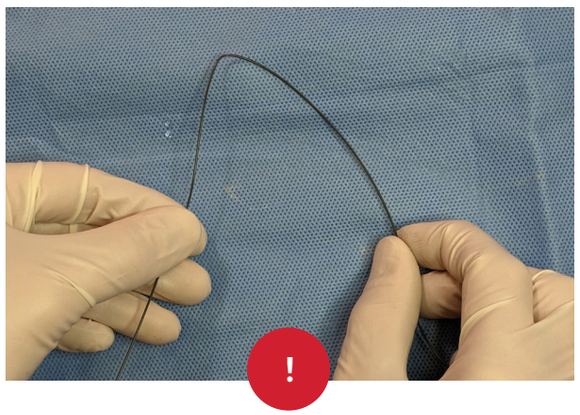
Prime the catheter by flushing the infusion hub of the device with heparinized saline until droplets of saline appear out of the distal tip.



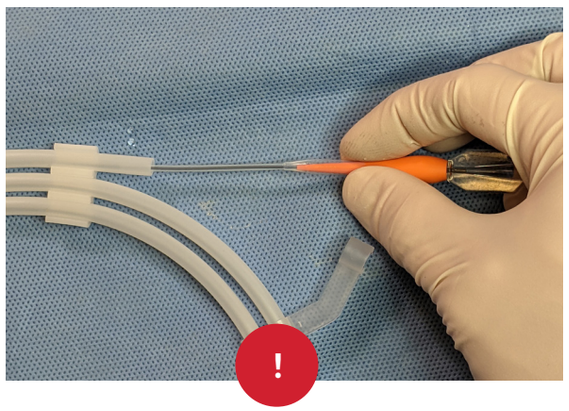
Prepare an appropriately sized guide wire according to the manufacturer's instructions for use. Carefully insert the guide wire into the infusion hub.



Carefully remove the infusion hub from the hub clip. Remove the catheter and the inserted guide wire from the coil dispenser tube.



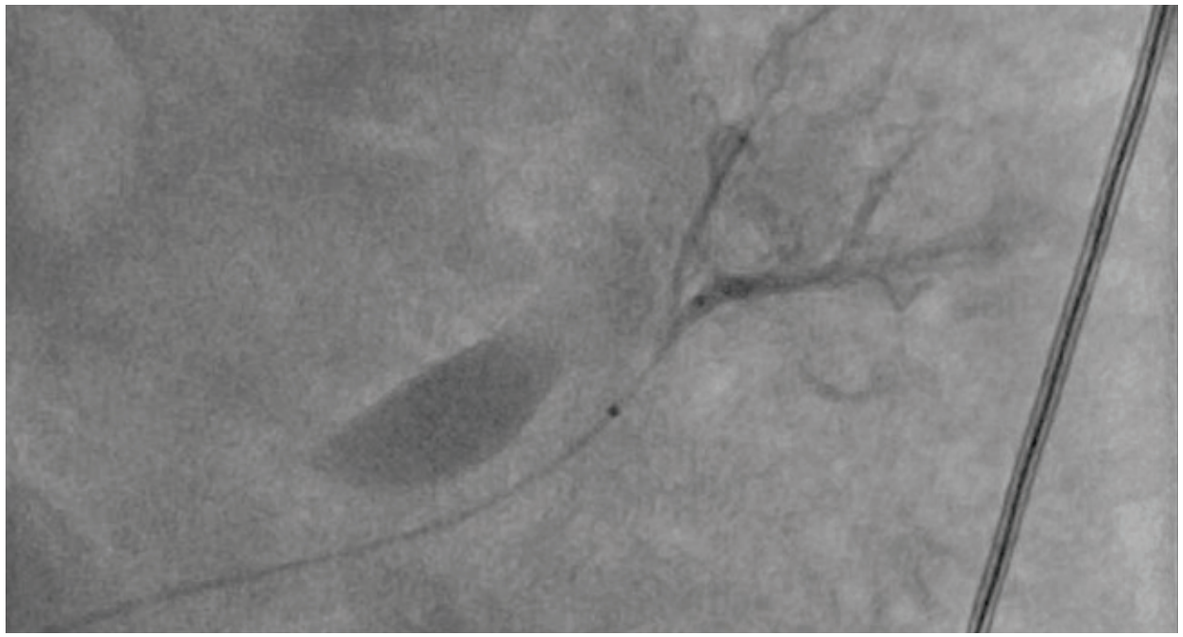
Avoid kinking the catheter.



Hold the Introducer and strain relief on the proximal end of the catheter. Pull as one unit and remove from the coil.

USING THE DEVICE

TRACK DEVICE TO TARGET LOCATION



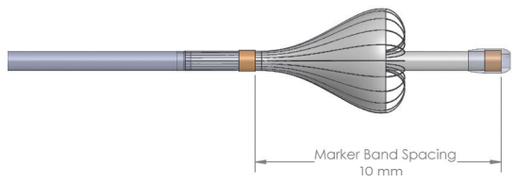
Track the device over the guide wire to the target location.

Note: It is important to adequately flush the infusion lumen throughout the procedure to prevent backflow of blood into the device lumen.

Note: There are two radiopaque markers on the distal end of TriNav. The most proximal band indicates where the protection starts.

Note: Position the proximal marker band past the desired protection zone.

Precaution: Maintain a continuous heparinized saline flush to achieve optimal device performance and prevent or reduce the risk of thrombus formation on the catheter and the self-expanding tip. The use of systemic heparinization to reduce the risk of thromboembolic complications should be considered for some patients, such as those with known hypercoagulable conditions.

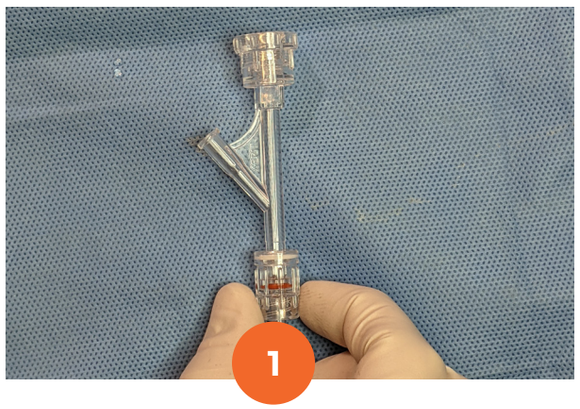


This is a continuous heparinized flush on the base catheter

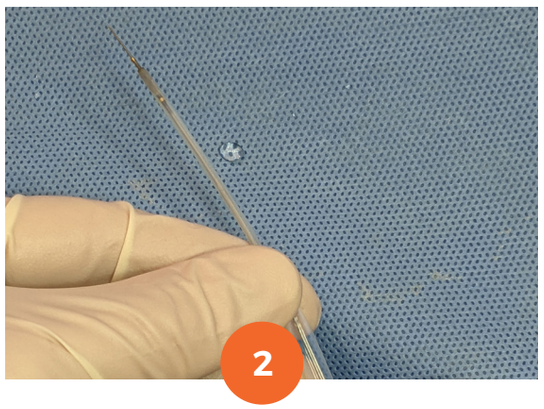
Warning: Do not advance, retract, or torque the device against resistance as this could cause vessel trauma, device damage, or breakage. If resistance is encountered while navigating the device, assess for vasospasm and treat accordingly.

Flush the infusion lumen and gently attempt to navigate again. If resistance is still encountered, carefully pull TriNav back into the base catheter and remove it from the patient.

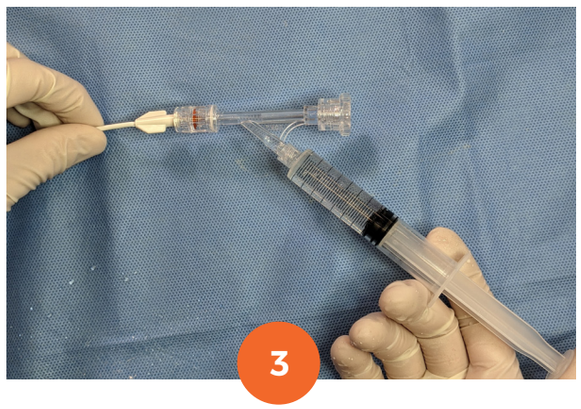
INSERTION INTO BASE CATHETER



Select a Tuohy-Borst with a y-connector to allow for adequate flushing of the base catheter during use.



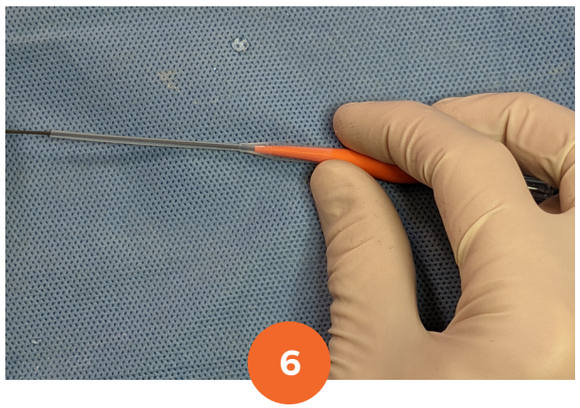
Carefully advance the provided Introducer over the SmartValve to facilitate insertion into the Tuohy-Borst adapter and base catheter hub.



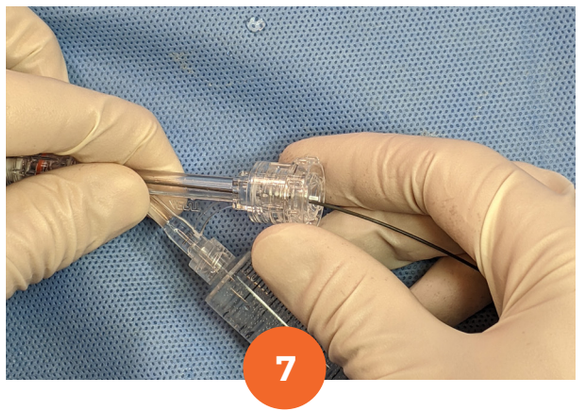
Flush the Base Catheter confirming the lumen is fully hydrated prior to inserting the device.

Insert the introducer through the Tuohy-Borst adapter and into the base catheter hub.

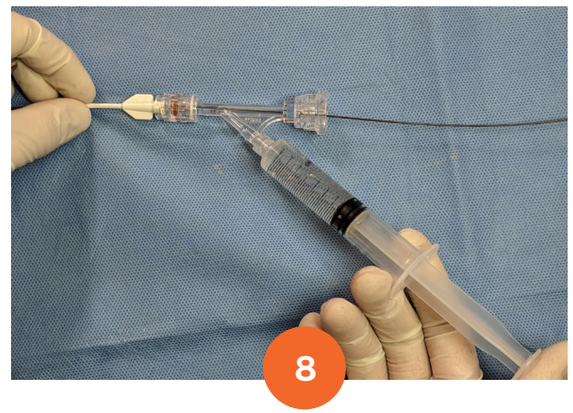
Carefully advance the device through the Introducer and into the guide catheter.



Withdraw the Introducer from the Tuohy-Borst adapter and move it to the end of the catheter.



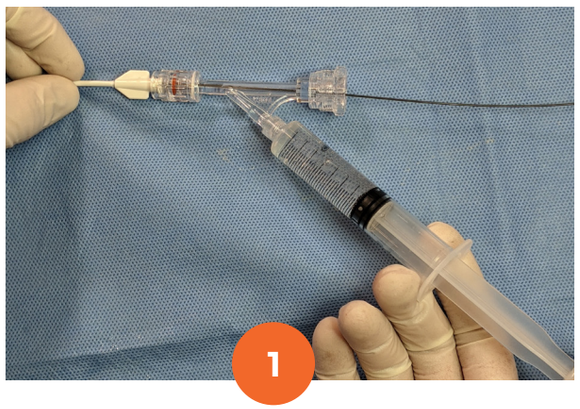
Tighten the Tuohy-Borst adapter around the catheter to prevent backflow while still allowing for movement of the catheter through it. Avoid over-tightening.



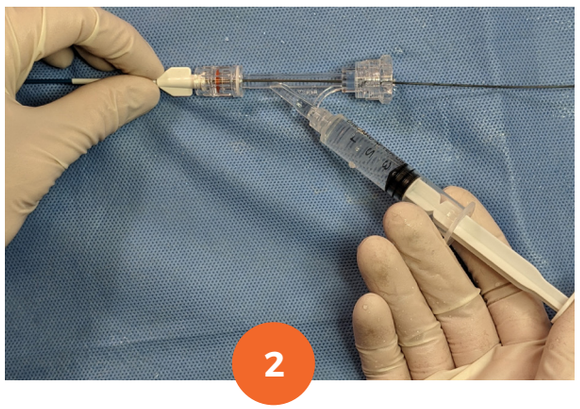
Use the y-connector on the Tuohy-Borst to **maintain a continuous flush of the lumen of the base catheter.**

MAINTAINING A CONTINUOUS FLUSH ON THE BASE CATHETER

HAND FLUSH



Fill a 5cc or 10cc syringe with heparinized saline and attach to the y-connector of the Tuohy-Borst.



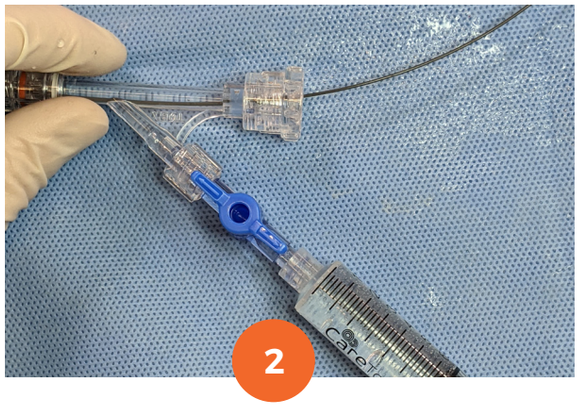
Flush the Tuohy-Borst and the base catheter with the saline by hand confirming that the lumen is fully flushed.

Repeat this every 5 minutes throughout the duration of the procedure or anytime that blood ingresses into the lumen of the base catheter, such as when the TriNav is moved or the valve on the Tuohy-Borst is opened.

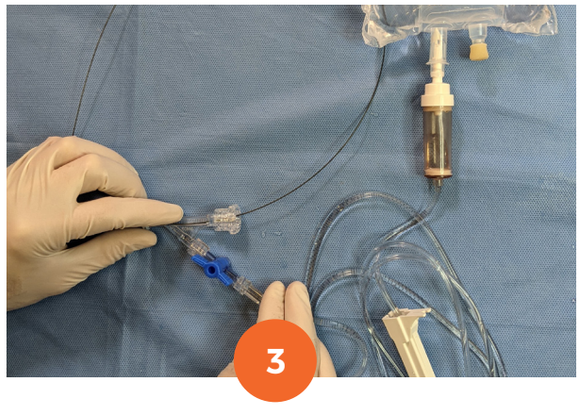
!

IV DRIP BAG

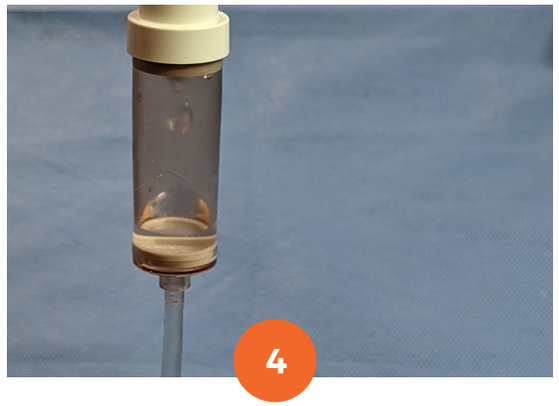
Setup an IV drip bag with heparinized saline confirming the volume of saline is appropriate for the duration of the procedure. Confirm all lines coming from the bag are flushed.



Flush and connect a 2-way stopcock to the y-connector of the Tuohy-Borst.



Connect the extension tubing from the IV drip bag to the stopcock on the y-connector and open the stopcock.



Pressurize the IV drip bag to the appropriate level. The bag should drip approximately once every second.

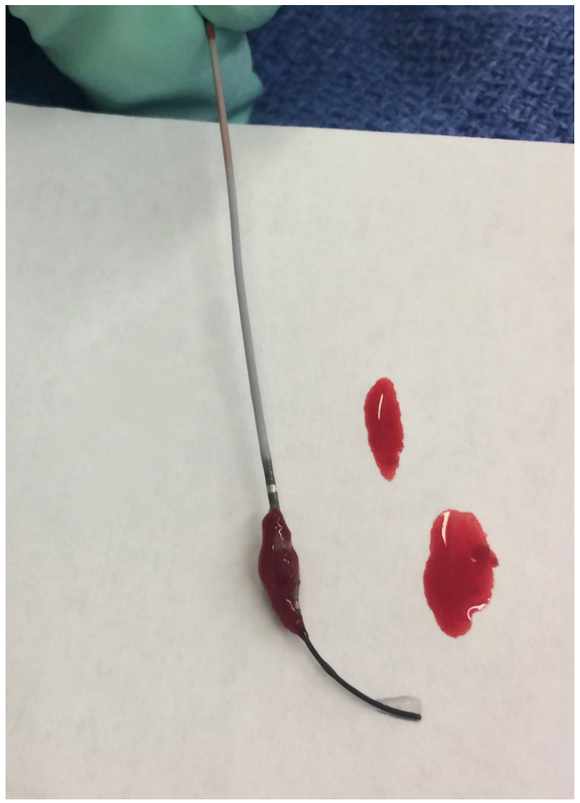
! **Confirm that all lines are cleared from high movement areas and secured to the patient as to prevent any interference with the extension line.**

Rx only. For the safe and proper use of the TriNav device, refer to the Instructions for Use.

IMPACT OF POORLY FLUSHING THE BASE CATHETER

When the lumen of the base catheter is not properly flushed, clot may accumulate inside the space between the TriNav and the ID of the base catheter.

This may result in the following issues with performance:



Unlike a microcatheter, **the SmartValve of the TriNav fills the lumen of the base catheter and may gather any thrombus deposited on the inner lumen**. When the TriNav is removed a clot may adhere to the tip preventing reuse of the device or causing dissatisfaction. When the TriNav is introduced, the clot may be pushed into the vasculature potentially causing problems with therapy delivery.

Due to spatial interference of the clot in the lumen of the base catheter, the TriNav may no longer be dimensionally compatible resulting an inability to successfully remove the TriNav from the base catheter or an inability to introduce the TriNav through the base catheter.

SmartValve relies on radial force of the tip to expand within the vasculature.

- Clot accumulation in the base catheter may adhere to the support structure of the braid when the TriNav is:
  - introduced through the base catheter
  - retracted into the base catheter
- This prevents full expansion or collapse of the SmartValve which may affect trackability and performance.

!

USING THE DEVICE

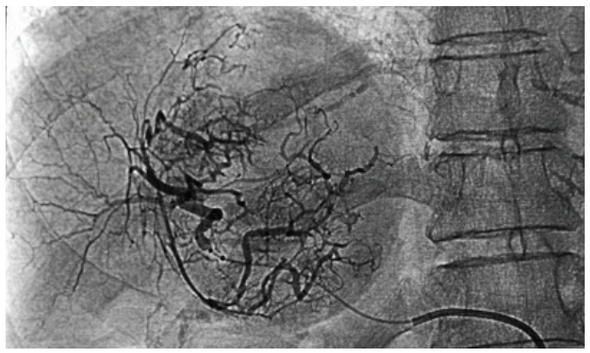
CONFIRM TIP PLACEMENT

1. Remove the guide wire.
2. Inject with contrast to confirm the infusion location and the apposition of the tip to the vessel wall under fluoroscopy. If repositioning is needed, reinsert the guide wire and reposition it as needed.
3. Always inject contrast through the infusion port to confirm its location prior to infusion of embolic agents.
4. Confirm that the contrast can be injected freely without excess pressure.
5. If the antegrade flow is less than desired, flush the infusion hub of the device, reposition, and reassess.
6. If there is contrast reflux, reposition and reassess antegrade flow.
7. Once the tip is positioned in the desired location, close the Tuohy-Borst adapter on the base catheter to prevent movement of TriNav. Do not over-tighten.
8. Adequately flush the infusion lumen with heparinized saline prior to the initial introduction of therapeutic agents.
9. If vasospasm is present in the target vasculature, treat accordingly prior to infusing therapeutic agents.
10. Infuse diagnostic, embolic, or therapeutic agents according to the manufacturer's Instructions for Use.

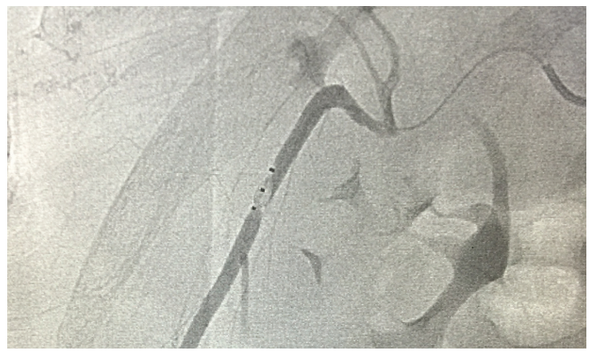
USING THE DEVICE

INFUSION END POINTS

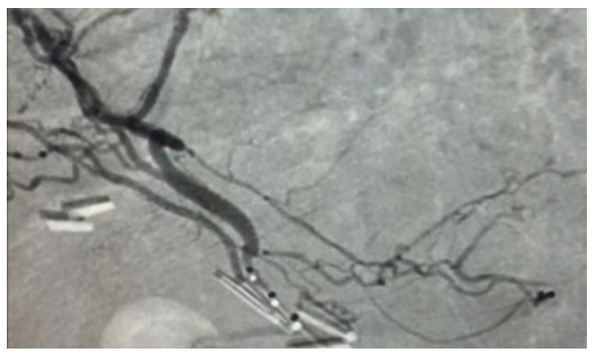
Prepare agent according to the manufacturer's instructions.



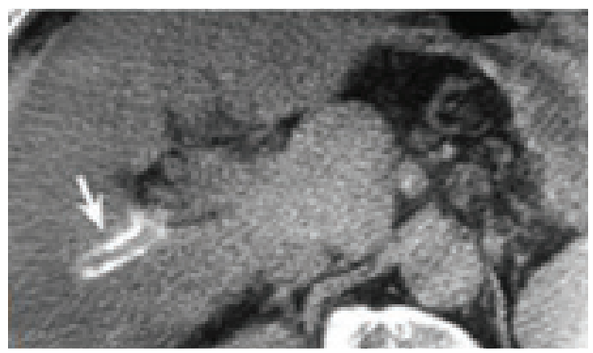
A. Full delivery of physician-prescribed agent



B. Retrograde leaching of contrast medium through the expandable tip[1,2]



C. Development of an intrahepatic collateral vessel leading away from the target tumor[1,2]



D. Visualization of the portal vein[1]

Note: Images are for reference only. Determination of the infusion end point is at the sole discretion of the physician.

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1 Titano et al Study Design: A retrospective, single-center study included 88 treatment-naive patients with solitary HCC tumors <6.5 cm who underwent treatment utilizing either SIS (n = 18) or standard EH microcatheters (n = 70). Twenty-three patients (5 SIS, 18 EH) received a liver transplant during the study, with 1 SIS and 6 EH patients excluded from the tumor necrosis analysis for receiving subsequent therapies prior to transplant. A pathologist performed a blinded review of the liver explant specimens to assess tumor necrosis and treatment distribution. Pathological analysis of explanted livers showed greater concentrations of microspheres within the tumor relative to the surrounding tissue in SIS explants (88.7 ± 10.6%) versus the EH explants (55.3 ± 32.7%) (p = 0.002). Titano JJ, et al. *Cardiovasc Intervent Radiol.* 2019;42:560-568.

2 Kim AY et al Study Design: Single center retrospective evaluation of patients who underwent DEE-TACE for HCC, delivered with SIS. Treatment response rates were assessed using the modified Response Evaluation Criteria in Solid Tumors criteria. A total of 22 patients with 39 separate HCC lesions underwent 28 treatments with SIS. Ten patients (45%) underwent de novo treatment with SIS whereas 12 patients (55%) were previously treated with a microcatheter. Complete response was demonstrated in 32% of patients and 54% of lesions after a single treatment session with the SIS. Overall disease response was demonstrated in 91% of patients and 85% of lesions after a single treatment. No grade 3 or higher elevation of alkaline phosphatase or total bilirubin was seen at follow up. Kim AY, et al. *PLoS One.* 2017;12(9):e0183861. DOI: 10.1371/journal.pone.0183861.

USING THE DEVICE

DEVICE RETRACTION

- Flush the Tuohy-Borst adapter on the base catheter.
- Open the Tuohy-Borst on the base catheter.
- Under fluoroscopic guidance, withdraw the device from the base catheter.

If the device will be used again within the same procedure, flush the infusion port, and keep it soaked in heparinized saline solution.

!

Warning: Do not advance, retract, or torque the device against resistance as this could cause vessel trauma, device damage, or breakage. If resistance is encountered while navigating the device, assess for vasospasm and treat accordingly.

Flush the infusion lumen and gently attempt to navigate again. If resistance is still encountered, carefully pull TriNav back into the base catheter and remove it from the patient.

TROUBLESHOOTING

Difficult or unable to infuse

- Assess for vasospasm. Address as required.
- Check the Tuohy-Borst adapter to ensure that it is not overtightened. An overtightened Tuohy-Borst can cause catheter occlusion.
- If applicable, examine for impingement along the Y-90 infusion lines.
- Check the hub for clumping or clogging.
- Confirm embolic sphere size is compatible.

Stasis develops almost immediately

- Assess for vasospasm. Address as required.

Reflux appears at the target location

- Assess for vasospasm. Address as required.
- Confirm the SmartValve size is appropriate for the vessel size.
- Reposition the tip and reassess.

Resistance is encountered when pulling the device back into the guide

- Do not retract against resistance as this could cause vessel trauma, device damage, or breakage.
- Assess for vasospasm. Address as required.
- Flush the base catheter to expel any blood from the lumen.
- If unable to resolve, pull TriNav and base catheter from the patient as a single unit.

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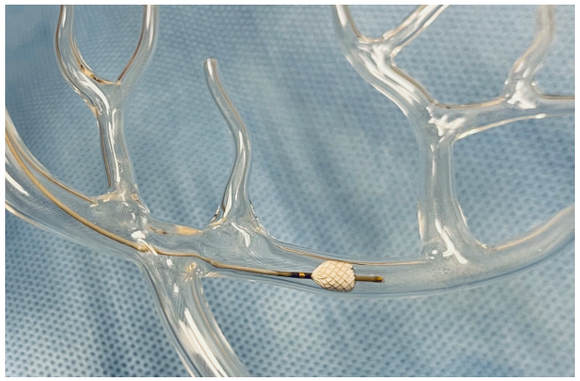
TIPS AND TRICKS

1. MAINTAIN A CONTINUOUS FLUSH ON THE BASE CATHETER

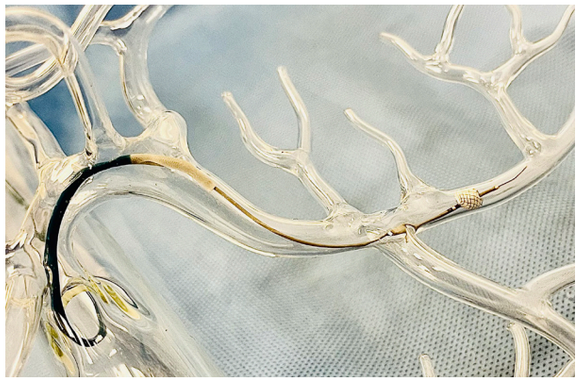
- Prevents clot buildup in the base catheter lumen
- Options for flushing: **See slide 7**
  - Hand flush periodically
  - IV drip bag

2. OVERCOME DIFFICULT TRACKING



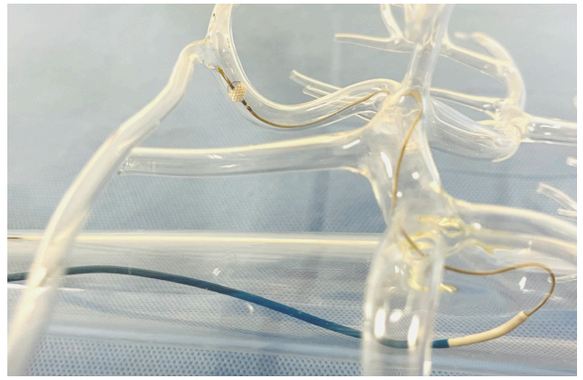
The TriNav tip consists of a super elastic nitinol valve that exerts radial force around the entire device. This acts to self-center the catheter within the vessel.

Recognition of this geometry within the vessels is important when troubleshooting difficulties in tracking the device.



Try to advance base catheter more distally in the common hepatic artery to increase stability during tracking.

Some shapes of base catheters can allow the physician to track the base catheter beyond the origin of the celiac artery which can provide additional support to the TriNav during tracking.



Base catheter backing out of celiac when tracking device

Getting more purchase with the base catheter anchors the base catheter in an area where the surrounding vasculature can provide additional support. With this additional support, the force required to track the TriNav does not come solely from the support provided by the shape memory of the base catheter.

The further the TriNav tracks out from the base catheter the more difficult it is for the supportive force from the base catheter to be directed to the device for the purposes of tracking. Getting more purchase will reduce this distance and provide more support from the base catheter.

TIPS AND TRICKS

3. CONSIDER A CHANGE IN WIRE

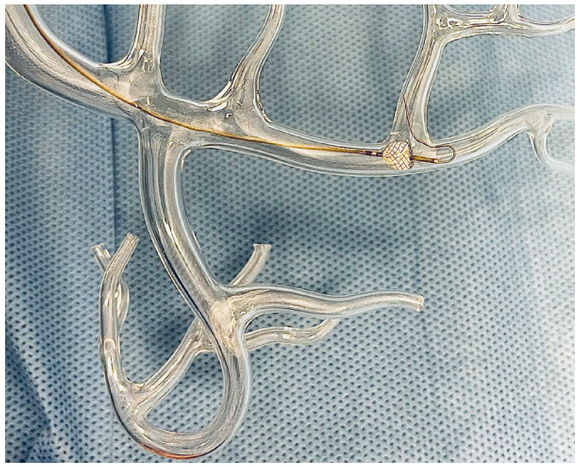
Use a softer wire to improve flexibility

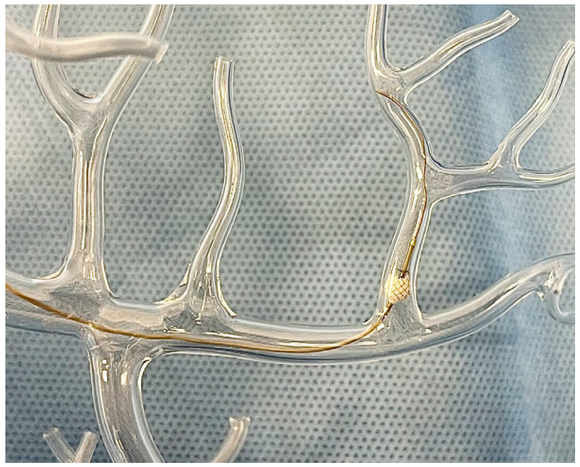
» This may allow the device to bend more easily around turns and may allow for more self-centering, allowing it to take more tortuous turns.

Use a stiffer wire to push past obstacle

» This may give the device more ability to push, preventing it from getting hung up in the vasculature and may deflect the tip from a centered position as the wire will exert more force on the tip.

Wire change techniques

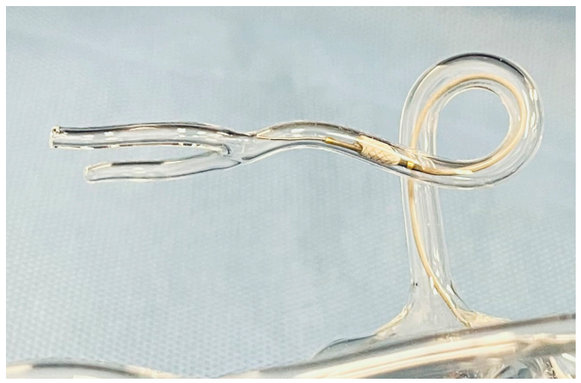




Attempt to place the wire further out in the vasculature giving the system more support and deflecting the tip from a centered position as the wire will exert more force on the tip.

Then pin the wire in place or slowly retract the wire while simultaneously advancing the TriNav to track the TriNav over the wire.

Ensure that the lumen of the TriNav is hydrated to enable smooth tracking over the wire.



Position the wire just past the end of the TriNav and advance both together as a system. This will allow for more self-centering and enhanced flexibility, allowing it to take more tortuous turns.

TIPS AND TRICKS

4. ADJUST FOR ANATOMICAL OBSTACLES

Omega shape prior to target location

- The omega shape as been noted as particularly difficult.
- Try a softer wire or move the wire to just past the TriNav and navigate as a system to minimize the force of the wire and allow the tip to self-center.
- This can displace the leading tip of the device away from the vessel wall, reducing resistance.
- Further, minimizing the stiffness of the wire minimizes the overall stiffness of the leading end of the device and allows it to take more severe turns.

Bifurcation

- The SmartValve of the TriNav can catch on a bifurcation.
- Recommend a stiffer wire or placing the wire further past the bifurcation and tracking over the wire.
- A bifurcation can be envisioned as an edge in a normally symmetrical vessel. The SmartValve will expand to fill the vessel, so it can extend across and catch on the edge formed by the bifurcation.
- The placement of a stiffer wire or advancing the wire more distally will cause the deflection of the expandable valve from the more self-centered shape to one lying more tightly against the wall of the vessel in which the guidewire is directed.
- This will reduce or eliminate valve resistance against the bifurcation point.

TIPS AND TRICKS

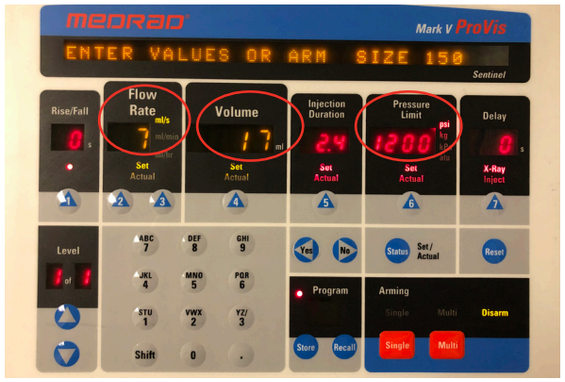
5. USE A POWER INJECTOR

Power injectors have a preset input flow and input volume, as well as a pressure limit

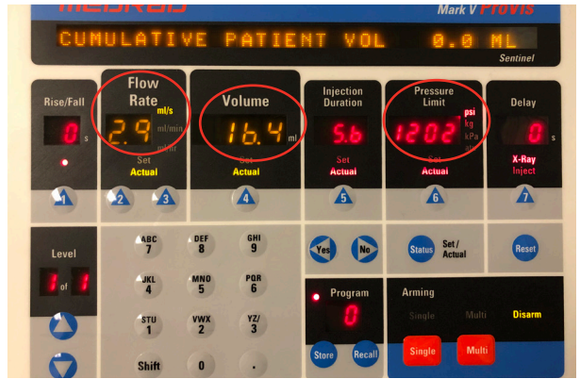
- They will attempt to inject at the programed flow rate unless the pressure limit is hit.
- If the pressure limit is hit, the injector will continue infusion at a lower rate that is at or below the pressure limit.
  - Therefore, the input flow rate is not necessarily the actual achieved flow rate and the pressure limit is not necessarily the actual achieved pressure.

FOR EXAMPLE If the Power Injector is set to a flow rate of 10mL/sec for 10mL but the pressure limit is set to 100 psi, the injector will limit the flow rate significantly so that it does not exceed 100psi. In this scenario, the actual flow rate may never achieve more than 1mL/sec. Alternatively, if the flow rate is set to 0.5mL/sec for 10mL but the psi limit is set to 1200psi, the injector will infuse up to the input flow rate but may never reach the pressure limit that was set.

The actual achieved flow rate, volume and pressure during the injection can be reviewed from the home screen of the Power Injector.



Setpoints



Actual Achieved Values

- This is important when comparing two systems that may have different resistances such as a different ID.
- Even if settings are the same it does not mean the power injector injected the same flow rate or the same pressure.

TIPS AND TRICKS

6. ENHANCING CONTRAST DURING MAPPING

Compare to a standard microcatheter

- **Verify that the flow rates are the same for the two systems.**
  - In order to accurately compare the systems, the ACTUAL ACHIEVED FLOW RATE must be the same, not just the input flow rate.
    - The physician may need to update the pressure limit settings on the high pressure injector to ensure it does not limit flow rate in the TriNav device.
    - If the actuals are still not matching, the physician may need to dilute the contrast with saline to reduce the pressure that is required to inject at a high enough rate with the TriNav to match the other microcatheter.
- **Verify the ID of the standard microcatheter.**
  - Catheters that have a larger lumen require less pressure to achieve an input flow rate.
    - If it is a “High Flow” catheter, it typically has a 0.027” ID whereas the TriNav has a 0.021” ID.
    - For example a 0.027” ID 130cm Progreat can infuse contrast at a rate of 3.7ml/sec at 750psi. The 0.021” TriNav can infuse contrast at 2.6ml/sec at 1200psi.

Inject with a high enough rate to cause reflux with a microcatheter.

- First verify that the rate in which you are injecting is causing reflux with the standard microcatheter then utilize the same rate to inject with the TriNav.
- The most pronounced differences between the systems will be visible if contrast is infused at a rate that is causing reflux with the standard microcatheter.
- The SmartValve on the TriNav is capable of generating pressure during injection, which directs flow into the distal vasculature that would normally reflux if using a standard microcatheter.
- This generates pressure which allows for penetration into the tumor and improved enhancement.

Move closer to the tumor.

- As a vessel becomes smaller, less injection rate is needed to achieve pressure enhanced contrast delivery.
- Getting closer to the tumor into the associated smaller vessels makes it easier to visualize the difference between the standard microcatheter vs a TriNav device.

In general, a 2ml/sec for 6ml or a 3ml/sec for 6-9ml setting seems to produce a pressurized response in most cases when using contrast.