Guide for the Implantation of Catheters in the Göttingen Minipig Using the Seldinger Technique

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Introduction

The main reason for using catheters in a minipig is to facilitate repeated serial blood sampling or intravenous dosing. It reduces the stress on the animal, improves the welfare and decreases the number of employees required for the procedure.

Although this method entails some risks and challenges, if properly managed it can be successfully executed after some training.

The purpose of this paper is to inform about the material and methods tested at Ellegaard Göttingen Minipigs and other Minipig users. They are subjective and by no means exhaustive.

Summary

There are several types of catheter that could potentially be used with a Göttingen Minipig. A central venous catheter (CVC) is, by definition, a catheter whose tip resides in the central circulatory system. It is often inserted in close proximity to the heart. A PICC is a peripherally inserted central catheter and a Midline catheter is peripherally inserted without ending up in the central circulatory system.

There are various manufacturers of catheters that can be implanted using the Seldinger Technique, each of which offers a multitude of models in different lengths, calibre, coatings, etc. They have single, double and multi lumen and almost all of them are made of PU. Common to all is that they are designed for humans and not for pigs, so it can be a bit tricky to find the model that suits a particular study best.

These types of catheters are intended for short-term use; the patency of the catheter can be anything between 3 and 28 days, depending on multiple factors.

The use of a dual lumen catheter, one lumen for dosing and the other for sampling, involves a risk of contaminating the blood sample with a compound as the two distal ports are close to each other. On the other hand using two lumens for sampling could provide an alternative if one lumen becomes occluded.

Catheterisation should be executed using aseptic procedures and under general anaesthesia, using the Seldinger technique or a modified Seldinger technique, at least one day before sampling. Use of a broad-spectrum antibiotic should be considered. The use of a needleless IV connection device (Bionector™) proved very useful.

Infections and a loss of patency are the main delayed complications whereas arterial puncture and impossibility to advance the guide wire are possible complications during insertion.

Although every effort has been made to ensure that the information contained herein is accurate, the author and the company which published this booklet waive all liability for its use.
Catheters

Commonly available catheters are designed for use in humans and are mainly used for fluid administration. Blood sampling is secondary. Due to different indications and anatomy, it has not been possible to find an ideal catheter for minipigs; compromises have to be made.

Different types of coatings (anti-thrombotic, anti-microbial) are also available, but the benefits are not conclusive in scientific literature. All manufacturers claim that their particular coating works and is the best.

Polyurethane (PU) is a commonly used material; different styles and makes are offered, with or without integrated extension, 1 to 3 openings and different flow rates. PU can be a bit stiff at room temperature but will soften at body temperature.

Catheters from several manufacturers have been tested, but as there are a multitude of different products not all were considered. Preferences are always subjective and are not based on extensive scientific studies.

Traditionally larger Göttingen Minipigs have been catheterised because lifting and handling becomes more challenging as age and thus weight increase. Therefore large-calibre catheters were used, but, as the procedure was applied in a broad spectrum of animal sizes and intentions, many different products were used.

The following list itemises the catheters successfully used in Göttingen Minipigs. It is based on user feedback, but is by no means complete. Most are single lumen; some have an integrated extension and others do not. You will probably have to try out a few to find the one that suits your taste and purpose.

For larger Minipigs > 15kg a 7 Fr catheter works fine, but for smaller pigs, the size has to be adjusted accordingly.
<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Calibre Ga/Fr</th>
<th>Length cm</th>
<th>Site used</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cook Medical</td>
<td>20/3</td>
<td>8</td>
<td>Jugularis/Saphena</td>
<td>C-PUM-301J</td>
</tr>
<tr>
<td>Edwards Lifesience</td>
<td>20/3</td>
<td>13</td>
<td>Jugularis/Saphena</td>
<td>M1 20130 HS</td>
</tr>
<tr>
<td>Arrow</td>
<td>14/7</td>
<td>16</td>
<td>Jugularis/Saphena</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18/4</td>
<td>20</td>
<td>Saphena</td>
<td>ES 04218</td>
</tr>
<tr>
<td></td>
<td>20/3</td>
<td>12</td>
<td>Jugularis/Saphena</td>
<td>AK 04150 E-S</td>
</tr>
<tr>
<td>Arrow</td>
<td>14/7</td>
<td>15</td>
<td>Jugularis/Saphena</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18/4</td>
<td>15</td>
<td>Jugularis</td>
<td>Certofix mono S145</td>
</tr>
<tr>
<td></td>
<td>18/4</td>
<td>20</td>
<td>Saphena</td>
<td>Certofix mono S220</td>
</tr>
<tr>
<td></td>
<td>16/5</td>
<td>30</td>
<td>Jugularis/Saphena</td>
<td></td>
</tr>
<tr>
<td></td>
<td>16/5</td>
<td>32</td>
<td>Jugularis</td>
<td>Cavafix certo 335</td>
</tr>
<tr>
<td>Braun</td>
<td>14/7</td>
<td>15</td>
<td>Jugularis</td>
<td>Certofix mono S145</td>
</tr>
<tr>
<td></td>
<td>18/4</td>
<td>15</td>
<td>Jugularis/Saphena</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18/4</td>
<td>20</td>
<td>Saphena</td>
<td>Certofix mono S220</td>
</tr>
<tr>
<td></td>
<td>16/5</td>
<td>30</td>
<td>Jugularis/Saphena</td>
<td></td>
</tr>
<tr>
<td></td>
<td>16/5</td>
<td>32</td>
<td>Jugularis/Saphena</td>
<td></td>
</tr>
<tr>
<td></td>
<td>13/7 (Dual lumen 16/16g)</td>
<td>30</td>
<td>Jugularis</td>
<td>Certofix duo V730</td>
</tr>
<tr>
<td>BD</td>
<td>20/3</td>
<td>15/20</td>
<td>Saphena/auricularis</td>
<td>Careflow 681639</td>
</tr>
</tbody>
</table>

General preferences:

- Integrated extension tube is preferable for the neck, as no extra extension is required. At other sites it is unwanted.
- No side holes reduces the risk of clotting/no washout of lock solution.
- Soft bevelled/rounded tip/softness.
- Small dead volume: reduces waste, rinsing.

Mila International ([http://www.milainternational.com/](http://www.milainternational.com/)) has a range of catheters and extensions designed for animals and are worth looking at.
The preferred insertion site is the jugular groove, entering the external jugular vein at a shallow angle (yellow arrows). This gives a penetration site where fixation is easy and the extension can be smoothly led away dorsally for effortless access later on. As the site is located between the legs and the mandible, where the neck has its lowest circumference, it is also the simplest site to bandage. This site also reduces the risk of puncturing the carotid artery.

In practice, successfully penetrating the vein proves to be quite difficult as only landmarks are available for guidance in many cases. Ultrasound-guided access is possible and will help a great deal in identifying the vein and cannulating it. Unfortunately the respective equipment is rather expensive and often unavailable.

The second penetration site (white arrows) is usually used for drawing blood samples. It is more difficult to bandage, there is a greater risk of finding an artery, and the inserted section of the catheter inserted is rather short (tip of catheter at the black line). On the other hand, venous access is easy, often by entering the vena cava. It is important to keep the angle of penetration shallow to avoid a kink in the catheter.
Ultrasound picture of external jugular vein with penetrating needle (arrow)

Position of transponder and needle during penetration

Kink in the catheter due to combination of a steep angle of entrance and movement of the head on day two after implantation.
Two different catheters entering vein
Site for tip placement

One concern about catheters with side holes is the necessity of advancing the catheter far enough inwards to ensure that the proximal opening is within the central vein. The distance from tip to last proximal opening on an Arrow® catheter is 2.5 cm.

Catheter Tip Placement, CVC

The catheter tip should be placed in the vena cava cranialis, just before the right atrium. The vessel diameter is large there, which reduces the risk of irritating the vessel wall, and blood flow is high. The catheter should not penetrate the right atrium to avoid complications. The following is a recommendation from the human sector:

“Probably the most important factor in the prevention of complications is the location of the catheter tip. The pericardium extends for some distance cephalad along the ascending aorta and superior vena cava. In order to guarantee an extrapericardial location, the catheter’s tip should not be advanced beyond the innominate vein or the initial segment of the superior vena cava. (It is important to note that a portion of the superior vena cava lies within the pericardium.) Some practitioners may prefer a deep SVC placement (within the lower third of the SVC), but nearly half the length of the SVC is covered by pericardial reflection that slopes downward toward its lateral edge. To avoid the risk of arrhythmias and tamponade, the tip of a CVC should lie above this reflection and not in the right atrium.”

(Source: QUICK GUIDE TO Central Venous Access, Edwards Lifesciences LLC)
There are three possibilities for checking the position of the tip:

- **X-ray/fluoroscopy**
  - Catheters are radiopaque and show up on x-rays. This is the most secure method as it verifies the position in situ but this equipment is not always available.

- **ECG**
  - When inserting the catheter, pull back the guide wire so that the end aligns with the tip, connect the guide wire to the RA lead (red in Europe, white in the US) and monitor lead II. When the central venous catheter is advanced from the jugular vein into the superior vena cava, the intra-atrial lead produces a normal P wave. As soon as the catheter tip reaches the sinoatrial node, there is an abrupt increase in the height of the P wave. When the tip enters the right atrium, the height of the P wave potential is reached. If the tip is advanced further into the atrium, the P wave declines again and becomes slightly negative. A negative P wave will be noticeable if the catheter tip is inadvertently advanced into the inferior vena cava. Slightly retract the catheter after you have seen an increase in the P wave to obtain the tip position desired.

- **Landmark**
  - The required placement of the tip can easily be established with this method. Put the pig in dorsal recumbency, hold a foreleg straight up and pull it slightly in a lateral direction. You will clearly see a tendon protruding. Draw a line on the sternum just caudal to the tendon. This landmark has been proven accurate by numerous necropsies. However it is only a landmark and does not take account of anatomical differences.
ECC of a minipig using the Nehb-Spoerri lead-placement measuring lead II. There is a clear change at the 8-cm length of insertion. Necropsy showed that the desired insertion would have been between 7 and 7.5 cm.
Landmark for positioning the catheter tip
Leg, midline catheter

The saphenous vein is usually prominent and visible in the Göttingen Minipig. The leg can easily be bandaged and as pigs are not very athletic it is impossible for them to interfere with their own bandage.

The disadvantage of this site is that there is some movement of the catheter along the vein as the minipig moves its leg (when walking or lying down). Whether this has a negative effect, like irritation or inflammation of the tissue concerned has not been tested.

A midline catheter can easily be placed at that site. The preferred technique is to gain venous access by placing an over-the-needle catheter first and then feeding the guide wire through this temporary catheter. If the guide wire has a J-tip, turn it around and use the straight end for this purpose. In an initial study, 18g 20 cm catheters were successfully used; the position of the tip was found to be in the area of the hip joint in a 12 kg minipig. Catheters were not in place for more than 3 days in these studies. Re-implantation at the same site proved to be impossible due to changes in the tissue around the site of insertion. Further studies using small calibre catheters are needed to see if they have the same effect on the vein and surrounding tissue. The use of longer catheters, so the tip rests in the caudal vena cava, could also be considered.
Saphenous vein with puncture site.

**Ear, midline catheter**

Some attempts have been made to insert a catheter into the auricular vein. It can be successful if the minipig is large and the vein well developed. A 20 g or smaller catheter is the only option here and even then the lumen of the vein is completely occupied by the catheter, severely reducing circulation through the vessel. This will cause tissue changes, and re-implantation is out of question. The small size of the vein makes it a difficult technique as well, compared to the other sites, as narrow corners have to be navigated during insertion. In a 15-kg minipig, the tip of a 15-cm catheter rests in the middle of the external jugular vein and with a 20-cm catheter, the tip rests just before the right atrium.
Catheter with Bionector valve sutured to the ear.

Path of the catheter from v. auricularis to v. maxilaris and v. jugularis with the yellow arrow indicating the bend where navigation of the catheter during insertion is difficult.

The auricular vein is completely filled out by the catheter and this complete vascular occlusion may be associated with significant alteration of the blood flow. Also necrosis or other histopathological changes of vessel tissue are possible side effects.
Seldinger Technique

This important technique for catheter placement was devised by Swedish radiologist S. I. Seldinger and is described in his paper of 1953. His apparently simple idea represented a big step forward, and his technique facilitates straightforward catheterisation of blood vessels.

The technique comprises three key steps: first, a hollow needle is inserted into the vessel to be catheterised; then, a guide wire is threaded through it and the needle is removed. The final catheter is then threaded over this wire and the guide wire removed to complete the catheterisation.

In the modified Seldinger Technique, an over-the-needle catheter or a peel-away introducer is used.

Placement of a catheter in the jugular vein:

1. Prepare and drape the site, then insert an introducer needle using an aseptic gloved technique.

2. Remove syringe.

3. Advance the “J” tip guide wire to the desired position in the vessel, using the distance markings provided. The “J” tip can be straightened for use in narrow vessels.

4. Withdraw the needle, keeping the guide wire position fixed.

5. Advance the vessel dilator over the guide wire and then remove it.

6. Place the catheter at the correct depth, using markings, and then withdraw the guide wire.
**Materials Required**

Catheter sets usually come in trays with all the items required for the procedure included.

- **Anaesthetic**
  - Zoletil 50
  - Xylazin
  - Ketamin
  - Butorphanol
  - 21 g butterfly, syringe for IM injection
  - Or according to preferred anaesthesia protocol

- **Preparation**
  - Ointment for eye protection
  - Ez-scrub - Iodine - Alcohol
  - Table with beanbag or V-bench
  - Hair clipper

- **Insertion**
  - Sterile gloves
  - Incise drape, or other draping
  - Catheter set
  - Scalpel 11
    - (Extension)
  - Syringes
  - Saline for flushing (20 IU/ml Heparin as an option)
  - Heparin/saline 100–500 IU/ml or other lock solution
  - Cap or Bionector® (Vygon) for catheter hub
  - Over-the-needle catheters

- **Fixation**
  - Suture (Prolene 2-0 Ethicon or similar)
  - Wound cover (Opraflex® or similar)
  - Bandage (Vetrap® or similar)
  - Tape (Tesa extra power universal or similar)
  - Polsterplast
Anaesthesia

Use the protocol you are most familiar with. The procedure from preparation to application of the bandage can take from 30 to 60 minutes depending on experience and the challenges encountered.
Our preferred protocol is:

1 bottle of Zoletil 50 dry matter  
(125 mg tiletamine + 125 mg zolazepam)  (conc. in mix: 12.5 mg/ml)
+ 6.25 ml Narcoxyl (xylazin 20 mg/ml)  (conc. in mix: 12.5 mg/ml)
+ 1.25 ml Ketaminol (ketamine 100 mg/ml)  (conc. in mix: 12.5 mg/ml)
+ 2.50 ml Torbugesic (butorphanol 10 mg/ml)  (conc. in mix: 2.5 mg/ml)

Dose: 1 ml per 10–15 kg pig IM  
Give an additional 1/3 of the dose if required
Keep refrigerated. Full effect for 1–2 months

This will give about one hour of deep narcosis.

Isofluran administered by facemask has been widely used for this procedure as well, however analgesia has to be administered separately as Isofluran has no analgesic properties.

Extensions

Depending on type of catheter, insertion site and size of the minipig, an extension to the catheter might be advisable to enable comfortable dorsal access. Some people choose a longer catheter to avoid using extensions. Extensions with integrated filters are not encouraged as they can block when aspiring.

Flushing, Locking and Lock Solutions

During catheter access, it is important to minimise the contact time of blood with catheter to reduce the tendency of biofilm or thrombi to accumulate. After collecting the blood samples, the catheter lumen should be flushed immediately with 0.9% saline. Do this by brisk injection to flush all traces of blood back into the circulation. Pulsating flushing might help to displace blood from the lumen of the catheter. Between the sessions of accessing a catheter, the lumen must be filled with a suitable solution to exclude blood and prevent the formation of thrombi. This process is called “locking”. The locking technique and solutions are also important to preventing infection. If the interval between experimental accesses of the catheter is prolonged, flushing might be necessary. Frequency of maintenance flushing is a balance between risk and benefit. When catheters are accessed, there is always a risk of pyrogenic or microbial contamination entering the bloodstream. With longer intervals between flushing, the risk of thrombi forming at the catheter tip increases.

Regardless of the amount and frequency of flushing, it is important to use a positive-pressure flushing technique. A proper positive-pressure flushing technique creates positive pressure within the lumen of the catheter and is believed to minimise the reflux of blood into the tip of the catheter, and thus prevent clotting. This flushing can best be performed by closing the catheter or extension clamp while flushing.
before the syringe empties completely. Another way to accomplish this is by maintaining pressure on the syringe plunger while withdrawing the syringe from the injection cap.

If there are any side holes in the catheter, it is also important to maintain firm pressure while flushing/locking to make sure the flushing also reaches the distal opening. However, make sure not to exceed the maximum pressure for which the catheter is designed. Use a large syringe: this will reduce the pressure in the catheter.

The most commonly used lock solution is saline containing heparin. The concentration of heparin in saline is rather empirical. References found in various scientific publications are in the range of 20–1000 IU/ml.

We have heard very encouraging reports from third parties using Taurolidine citrate.

**Catheter lock solutions**

<table>
<thead>
<tr>
<th>Lock solution</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% saline</td>
<td>• Enables filling of the catheter without exogenous chemical matter</td>
<td>• Does not prevent thrombosis</td>
<td>• Continuous low rate of infusion is effective in maintaining catheter patency</td>
</tr>
<tr>
<td></td>
<td>• Cheap and easy to obtain</td>
<td>• No antibacterial activity</td>
<td></td>
</tr>
<tr>
<td>0.9% saline with heparin (20–1000 IU/ml)</td>
<td>• The most widely used material, with heparin providing the thrombosis prevention</td>
<td>• Provides no antibacterial action</td>
<td>• Low concentrations for frequent flushing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Higher concentration for less frequent flushing</td>
</tr>
<tr>
<td>40% dextrose (glucose)</td>
<td>• The high osmolarity prevents bacterial colonisation and multiplication</td>
<td>• Risk of crystallisation</td>
<td>• Adding heparin (100–500 IU/m) will increase the prevention of thrombosis</td>
</tr>
<tr>
<td></td>
<td>• The high osmolarity contributes non-specifically to clot prevention/disruption</td>
<td>• The viscosity of the solution helps to prevent blood accessing the catheter lumen (but makes the lock solution slightly more difficult to withdraw)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Dextrose occurs naturally in the blood and is rapidly metabolised</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Available cheaply as a pharmaceutical formulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>46% sodium citrate</td>
<td>• A cheap antithrombotic which can be used where heparin is contraindicated</td>
<td>• Heat labile, therefore cannot be sterilised by autoclave</td>
<td>• Commercially available under the name DuraLock-C®</td>
</tr>
<tr>
<td>6.7% taurolidine citrate solution</td>
<td>• Taurolidine is an effective and convenient antibiotic</td>
<td>• Expensive</td>
<td>• Supplied commercially for catheter locking in preclinical research</td>
</tr>
</tbody>
</table>
Bionector® www.vygon.com

Bionector is a seven-day/150 access, closed, needle-free IV access system, which minimises the risk of infection and eliminates the risk of needle-stick injury during IV access. Once a Bionector is in place, you can infuse, inject and sample blood and change your IV tubing without opening the IV system, thereby enhancing safety and sterility.

The system is ideal for use in animals and allows easy, repeated IV connection and disconnection, regardless of how uncooperative the patient is.

Once a Bionector is connected, you can infuse, inject and sample. Its protective membrane automatically opens the fluid pathway only when a male luer has been fully inserted. When you disconnect the male luer, the protective membrane automatically seals the fluid pathway.
Procedure for Jugular Vein Placement

1. Prepare the pig for surgery
   - anaesthetise according to chosen protocol
   - apply eye ointment
   - shave around the neck
   - wash the pig thoroughly
   - mark the position of the right atrium with a pen (length of catheter)
   - disinfect the skin.

2. Aseptic procedure
   - drape (Steridrape® or similar)
   - penetrate the skin and find a vein, good flow
   - insert guide wire to required length, compare to landmark
   - remove needle (with syringe), leave wire in place
   - use dilator to extend opening, use of scalpel is an option
   - remove dilator
   - measure depth of catheter insertion (scale on catheter)
   - (prime catheter with 20 IU/ml of heparin in saline)
   - thread catheter over guide wire, making sure the end is protruding at hub
   - insert catheter with a twisting motion to required length
   - remove guide wire
   - check patency and flush with saline
   - attach Bionector®
   - suture wings to skin, extra clamp might be necessary.

3. Bandage
   - attach extension if necessary
   - apply wound dressing
   - bandage pig with Vetrap®
   - secure with duct tape
   - check patency and flush with saline
   - lock catheter with lock solution (heparin, Taurolock™, DuraLock™, etc.).
Dressing and Bandaging

Attach the extra clamp close to the penetration site, making sure kinks are avoided. If no extra fixation device is available, you can make your own using two pieces of tape, with the adhesive sandwiching the catheter. Cover the whole area with Opraflex® or another membrane with a high moisture-vapour transmission rate.

The conical shape of the pig’s neck makes it slightly difficult to bandage. Depending on the catheter entrance site, it is not always possible to cover it well. A flexible material like Vetrap® is advised, and there is no need to wrap it too tightly as it is only meant as protection. It helps to create a pocket of sorts where the catheter hub can be placed when not in use and easily taken out for access.

The application of duct tape has been very successful in preventing bandage edges from curling.

Check patency again at the end of bandaging to make sure the catheter and the extension are properly positioned within the bandage.

After a few days, the covering can shift or loosen, so check regularly to see if it needs to be replaced.

Depending on the pig’s temperament, anaesthesia might be necessary for re-bandaging. As there is vascular access, the use of Propofol is an option.
Alternative Dressing and Bandaging Material

The following combination of bandaging material has also been used successfully.

Instead of Opsite® use Fixomull® stretch cut to size and edges rounded
Vetrap® use Mollelast® haft
Duct tape use Optiplaste®-C

The actual bandaging is done in a similar fashion.
Procedure for Saphenous Vein Placement

4. Prepare the pig for surgery
   - anaesthetise according to chosen protocol
   - apply eye ointment
   - shave the leg
   - wash the leg thoroughly
   - disinfect the skin.

5. Aseptic procedure
   - drape
   - make a small incision in the skin over the vein
   - place an over-the-needle catheter in the vein; good flushback
   - mark the length of the catheter on the guide wire (tip at straight end)
   - insert guide wire with the straight end through temporary catheter, ca. 5–7 cm
   - remove temporary catheter, leave wire in place
   - use dilator to extend opening
   - remove dilator
   - (prime catheter with 20 IU/ml of heparin in saline)
   - thread catheter over guide wire, making sure the end is protruding at hub
   - insert catheter with a twisting motion into the vein
   - advance catheter so the tip protrudes from the guide wire by a few mm
   - advance catheter and guide wire together carefully the whole length.
   - remove guide wire
   - check patency and flush with saline
   - attach Bionector®

6. Bandage
   - apply wound dressing
   - put padding under the hub
   - tape hub
   - bandage pig with Vetrap®
   - secure with tape
   - check patency and flush with saline
   - lock catheter with lock solution (Heparin, Taurolock™, DuraLock™, etc.).

Wound dressing, padding and tape in place
Wrapping with Vetrap
Sampling and Catheter Maintenance

Use clean gloves for all catheter handling and disinfect the hub before and after every access to avoid infection.

Drawing blood can be done by syringe or vacutaniner with a luer adapter. The use of a syringe allows for better control of the withdrawal process.

Discard a certain amount of blood prior to blood sampling (the discard volume) to avoid contamination of laboratory samples with heparin or saline. The amount of blood drawn to clear the line depends on several factors, including:

- tubing size and length,
- amount of heparin in the line,
- the type of study to be performed.

This volume is often expressed as multiples of the dead space within the catheter. This is a function of the volume contained in the catheter from the tip of the catheter to the port from which the sample is to be drawn. Anywhere from two to ten times the dead space has been advised. To reduce waste, if the total amount of blood to be drawn is high, it is possible for the rinsing to be done by moving blood back and forth in the catheter, after the initial discard of blood, but bear in mind that there is a contamination risk with regard to the lock solution.

Flush immediately with saline after drawing blood to avoid prolonged contact with blood on the inside of catheter. The flushing volume should be two to four times the dead volume.

Always use a positive-pressure technique for flushing and locking.

If the intervals between sampling are short, it is sufficient to flush with saline, whereas longer periods and overnight demand a lock solution. Idle catheters should be attended to daily as follows:

- disinfect hub/Bionector®,
- draw a small amount (at least twice the dead volume) of blood and discard,
- flush with saline,
- lock with slightly more than the dead volume. If you have a catheter with lateral openings make sure you have enough pressure to fill it all the way to the proximal opening,
- disinfect the hub/Bionector®.

Check for infection on a daily basis and check to see whether the bandage is causing discomfort. To palpate the insertion site, use sterile gloves.
Possible complications

Complications at Insertion

Arterial puncture
Arterial Puncture can easily occur due to arterial and venous proximity, as well as variable venous anatomy and a lack of visual guidance. If bright red, pulsatile blood appears, applying local pressure may be enough to stop the bleeding.

Use the other side for the second attempt.

Tracheal puncture and air embolism may also occur in rare instances.

Difficulties in advancing the guide wire
Impossibility to advance the guide wire can occur (there should be no resistance whatsoever inserting the wire). This can have several causes depending on the depth of insertion. If the insertion is as far as the needle, then the needle is probably not in the vessel any more. (Remove the guide wire, attach the syringe and relocate the vessel.) Or it could be a mechanical problem (check the equipment).

If the wire has advanced beyond the needle, then the J-tip might be stuck in a small branch. (Carefully retract the wire slightly and turn it before advancing again. Retracting the wire can cause it to be damaged by the sharp edges of the needle. Never use force to advance and, if no progress is made, withdraw the wire together with the needle to avoid damage.)

Sometimes, repositioning the head leads to success. Remember that the anatomy and paths of the veins are subject to variation. In older pigs, veins can form islands, exemplified by the observance of three jugular veins in one location.

CT Scan of the veins in the Neck
Images courtesy of Christine Müller Charité Universitätsmedizin Berlin

CT Scan of vein - islands
Three major veins in the neck

**Systemic changes**

Arrhythmias are usually related to over-insertion of guide wire or catheter, with impingement of the tips of these devices in the region of the right bundle branch.

Cardiac tamponade: fluid in the pericardial cavity can be caused by the perforation of structures by a catheter or guide wire – the most serious condition (euthanasia).
Delayed Complications

The most common delayed complications of vascular-access device insertion are thrombosis and infection. These two complications are somewhat related, as thrombotic complications are common in catheterised veins and are often associated with catheter sepsis.

Thrombosis

All catheters are thrombogenic. Within seconds after insertion, much of the catheter body is coated with body fluids and proteins. Platelets adhere and thrombi form. Catheters can become encased within 5–7 days, forming a fibrin sheath. Mural (wall) thrombi may form on the catheter and/or on the wall of the vessel.

Catheter occlusion

Catheter occlusion can result from the formation of a fibrin sheath and/or thrombi at the tip of the catheter, but has also been associated with blood clotting, lipid deposits or precipitates within the catheter lumen. Fibrin sheath formation is significant in that the sheath may eventually encase the catheter completely and affect the functional ability of the catheter. Withdrawal occlusion may occur if the fibrin sheath acts as a flap blocking the tip of the catheter when the drawing of blood is attempted, and then opens up with injection.

Venous values can also interfere with sampling. The first step with a blocked catheter is always to reposition the animal and manipulate the catheter trying to move the tip to another location.

Often blockage is due to a slight or severe kink in the catheter or extension. Try to reposition the animal or remove the bandage to check. Attempts to clear catheter occlusions include the use of fibrinolytic agents or gentle pulsating suction.

Fibrin sheath/thrombi formation at the tip and inside after being in place for eight days.

Infection

We recommend that a strictly aseptic insertion technique be used. At times, suboptimal conditions can prevail, in which case the use of antibiotics is indicated. A broad-spectrum antibiotic like Noropen or Noropen Prolongatum Vet could be used. For the latter, injection at insertion time is sufficient.
Catheter-related bloodstream infection can be due to hub contamination and is the most likely mechanism for infection occurring in long-term catheters with repeated manipulation. Skin contamination and the migration of dermal organisms through the cutaneous catheter tract is the most likely cause of infection in the short term.

Aseptic techniques and hub disinfection are imperative. The use of a Biopatch® (Ethicon360) may prevent infection.
Catheter Replacement

There can be many reasons for replacing a catheter, including infection or occlusion. Replacement over wire is a fast and easy method but is contraindicated when infection is detected or suspected. With this technique, the guide wire is inserted through the line in place, followed by the removal of the old catheter and its replacement with a new one.

Extreme care should be taken as there is the possibility of loosening a thrombus or pushing it into the bloodstream, especially if a catheter is occluded.

Catheter Removal

Depending on the temperament of the animal, anaesthesia is not required for removal. Clip the sutures and pull out the catheter with a smooth steady motion. Apply pressure for two minutes. Observe an aseptic technique.
Conclusion

The use of catheters is a valid option for repeated serial blood sampling, even though it poses some risks and challenges. Surveys from the human medicine sector show that even with the best equipment and well-trained personnel, the success rate is only 90%.

The greatest variety we found is in the duration of patency: this depends on many factors and is not easy to control. This led us to conclude that replacing a catheter is better than having to maintain an idle catheter over a long period of time and risk losing patency.

Of course, there are numerous factors to consider, as well as weighing the risk, cost, benefit and animal welfare issues, before reaching a decision regarding whether to use this method.

This guide is meant to help you with this process. We welcome any input you have if you wish to share your catheter experiences, as this will improve our guide for the benefit of others.
Placement of a CVC by Peel-away Introducer

by
Abdullah Kandira, Diana Ströbel, Birgit Alka, Carolin Joerg, and Dr Gabi Itter, DSAR-ARW SANOFI, Germany

A chronically implanted large-animal model as refinement and reduction in research: percutaneous venous catheterization in the Gottingen Minipig

There is a need for repeated long-term serial blood sampling and continuous infusion for pharmacological studies. Swine are commonly used as large animals for various experimental studies. The similarity in many aspects of anatomy, physiology and biochemistry to the human being is well documented.

In drug development and pathophysiology, there is an increasing demand for chronic large-animal models with permanent vascular access for serial pharmacological and pharmacokinetic studies. Minipigs are often used in research due to their size and easy training features. We recently started “PRIT” – positive reinforcement training – to make handling easier and less stressful for pigs and researchers. The Ellegaard Göttinger Minipig was chosen as an animal model for the cannulation of the v. jugularis for the use in studies involving repeated blood-sampling.

Göttingen Minipigs were anaesthetized and percutaneously catheterized with a guide-wire technique (CAVAFIX®) using palpable anatomical landmarks, triangulation and an intraoperative x-ray check. This minimally invasive catheterization allowed our researchers to obtain blood quickly and easily via central venous access. The technique has the advantage of minimizing damage to soft tissue and blood vessels. We adapted this procedure by using five anatomical landmarks to target and catheterize the external jugular vein in pigs. Intra-operative check of the position of the catheter-tip is routinely performed via x-ray.

Percutaneous catheterization of the external jugular vein can be accomplished easily in most pigs by using this technique.

Catheters are usually left in place for a period of three weeks or as long as they are patent. 70% of the implanted catheters were still patent after 21 days. They were rinsed with saline and locked with TauroLock HEP 500 on a daily base during idle time.

Conclusions: the Model of percutaneously catheterized Minipigs by using the (CAVAFIX®) technique contributes to the 3Rs of research

• Refinement: Catheter implantation technique allow serial studies in the same animal (placebo and drug can be evaluated in one animal after a washout period)
• Reduction: Due to re-use in repetitive experiments, fewer animals are needed
• Refinement: Due to chronic instrumentation
• No need for anaesthesia during PK/PD Study
• No influence of experiments through anaesthesia
• Conscious animals show physiological behaviour during studies
• Refinement: Due to training of the animals according the study outline (PriT), improvement of the surgical implantation technique and the use of appropriate materials with respect to animal welfare, repeated studies and catheter compatibilities (i.e. size, material, tips and lockings, implanted length, port and catheter maintenance, time interval of catheter flushing, reproducibility, user friendliness).
Minipig – Central Venous Catheter Implantation “Cavafix Certo with Splittocan”

**Equipment:**

**Preparation:**
- Endotracheal tube
- Laryngoscope with a long spatula
- Eye ointment
- Intravenous catheter

**Catheter insertion:**
- Cavafix Certo® with Splittocan® 338, 1,1x1,7 mm/16 G, length: 32 cm, Braunüle 1,8x2,35 mm/14 G, Production: Braun Melsungen)

- Bionector

- 1x tissue forceps
- 1x ligature scissor
- 1x needle-holder
- 2x 10 ml syringe with NaCl
- 1x 10 ml syringe
- sutures
- sterile gauze
- sterile surgical drapes
Bandage:
- Iodine ointment
- Fixomull stretch
- Mollelast haft
- Optiplast tape
- Tesa tissue tape

Anesthesia:

Introduction:
- Zoletil (Tiletamin/Zolezepam) dissolved in 10 ml Xylazin 0.5ml–1ml / 10 kg i.m.
- Propofol 1% 1–2 mg/kg i.v. (if required)

Inhalation anesthesia:
- Isofluran 0.3–1 vol. % (close monitoring of vital parameters)

Devices:
- Pulse oximeter
- Anaesthesia equipment
- ECG
- Heat mat

Implantation:
- Anaesthetize the animal with Zoletil in the animal room
- Transfer the Minipig to the surgical preparation room
- Insert intravenous catheter into ear vein
- Connect the pulse oximeter to tail, ear, tongue or udder teat
- If required, Propofol for intubation
- Intubation after anaesthesia in the prone position
- Connect the anaesthesia equipment
- Protect the eyes from drying
- Shave and disinfect the neck area
• Transfer the pig to the surgery room
• Place in the supine position
• Connect the pig to the monitoring devices
• Disinfect the surgical area
• Localize the surgical area generously with sterile drapes

• Select the site for puncture (triangulation technique - W. S. Flourney, S. Mani) and insert the needle under aspiration (negative pressure in the syringe)

• Puncture the vessel
• Blood should be easy to obtain
• After puncturing the vein, withdraw and remove the needle

• Connect the yellow connector to the plastic cannula and insert the catheter

• After positioning the catheter, remove the red sheath from the yellow coupling piece and tear the protective sheath

• Remove the two-piece yellow connector
• Introduce the catheter completely and split the plastic cannula

• Aspirate blood for testing
• Check the position of the catheter tip using x-ray
  (Cavafix Certo with Splittocan has a RadiOpaque stylet)

• Affix the catheter with tape and ligatures
Dressing:

- Connect the Bionector to the catheter
- Affix the catheter close to the puncture site with an adhesive plaster (Fixomull stretch)

- Wrap first with Mollelast Haft
- Secondary dressing with Optiplast tape (self-adhesive for good fixation)
- Affix the end of bandage with black Tesa tissue tape
References

1. Percutaneous external jugular vein catheterization in piglets using a triangulation technique. W S Flournoy, S Mani in Laboratory Animals (2009)