

Video Article

# Femoral Arterial and Venous Catheterization for Blood Sampling, Drug Administration and Conscious Blood Pressure and Heart Rate Measurements

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## Abstract

In multiple fields of study, access to the circulatory system in laboratory studies is necessary. Pharmacological studies in rats using chronically implanted catheters permit a researcher to effectively and humanely administer substances, perform repeated blood sampling and assists in conscious direct measurements of blood pressure and heart rate. Once the catheter is implanted long-term sampling is possible. Patency and catheter life depends on multiple factors including the lock solution used, flushing regimen and catheter material. This video will demonstrate the methodology of femoral artery and venous catheterization of the rat. In addition the video will demonstrate the use of the femoral venous and arterial catheters for blood sampling, drug administration and use of the arterial catheter in taking measurements of blood pressure and heart rate in a conscious freely-moving rat. A tether and harness attached to a swivel system will allow the animal to be housed and have samples taken by the researcher with minimal disruption to the animal. To maintain patency of the catheter, careful daily maintenance of the catheter is required using lock solution (100 U/ml heparinized saline), machine-ground blunt tip syringe needles and the use of syringe filters to minimize potential contamination. With careful aseptic surgical techniques, proper catheter materials and careful catheter maintenance techniques, it is possible to sustain patent catheters and healthy animals for long periods of time (several weeks).

## Video Link

The video component of this article can be found at <https://www.jove.com/video/3496/>

## Protocol

### 1. Prior to Starting Surgical Procedure

**Note:** Prior to beginning any animal procedures ensure that you have obtained the appropriate permission through your institution/organization. As with all survival surgeries, make sure that the surgery is performed under sterile conditions and the appropriate pain medication and antibiotics needed are used for a successful outcome.

1. Prior to beginning the catheterization procedure evaluate the catheters by flushing them with sterile saline to ensure they are patent.
2. Anesthetize the rat.
3. Prepare the rat for the surgical procedure.
  - a. Shave the fur from the surgical regions, which include the back of the neck (between the shoulder blades) and the inner leg region.
  - b. Using Betadine and a 70% ethanol scrub respectively, scrub the shaved surgical regions starting in the center and making a circular sweep outwards. Repeat this 3 times for each region, finishing with a final cleansing with 70% ethanol.
  - c. Place the animal on a sterile surface and place sterile drape over surgical areas. (The use of Press-n-Seal is an ideal surgical draping allowing the investigator to monitor the animal throughout the procedure.)
4. Ensure all surgical tools for the surgical procedure have been sterilized.

### 2. Preparation of Surgical Areas for Catheter Placement

1. With the rat laying prone (on its stomach), make approximately a ½ inch (12 mm) horizontal incision on the back of the neck at the level of the shoulder blades with scissors or a scalpel, then blunt dissect a subcutaneous "pocket" in the back approximately the size of a quarter. This will be used as an area to place a small amount of tubing that will compensate for animal growth and/or movement, i.e. so that the catheter isn't pulled on and thus removed from the artery it was placed in. (Alternatively this step can be performed immediately prior to tunneling the catheter.)
2. Place the rat onto its back (supine position) and make an incision in the inguinal area [approximate ½ inch (12 mm) incision along the natural angle of the hind leg.

3. Blunt dissect to separate the connective tissue (Figure 1) (can use blunt-tip scissors, hemostats, cotton swabs, etc.) (typically by holding your blunt tipped scissors and/or cotton swabs at a 45 degree angle this ensures the easier localization of the region of interest) until the femoral artery and vein are exposed.
  - a. The vein is dark red in color and the artery is clearer and brighter than the vein. The nerve that runs along the artery is whitish in tone.
4. Blunt dissect in the leg region to make a small open region below the skin (i.e. pocket, approximately the size of a quarter) along the inside of the leg for placement of a small section of the catheter (again to take into account animal movement and growth of the animal if chronic placement).
5. Place the retractors into the incision area so that you can fully view the artery and vein.
6. Using fine tip forceps gently separate the nerve (whitish in color) that is along the femoral artery away from the artery and vein. (Figure 2) Be careful to not cut or damage the nerve.
7. Separate the artery and vein as one unit, trying to expose an approximately ¼ inch (5-7 mm) length section of artery/vein.
8. Repeat the process in separating the vein from the artery. Keep your surgical instruments (i.e. fine tip forceps) perpendicular to the vessels and separate the vessels in parallel. This assists in avoiding tearing, pricking or damaging the vessels. By placing the fine tip forceps gently between the artery and vein from underneath and slowly opening the forceps and repeating this, you will slowly separate the vessels. Note: if you do tear or observe some bleeding use a sterile cotton swab and/or 2 x 2 gauze and place pressure on the area until the bleeding has stopped, then continue with the surgery.

### 3. Tunneling the Catheter

1. Place sterile saline soaked 2 x 2 gauze over the incision and turn the animal to its stomach.
2. Place the Rochester Pean forceps (long straight forceps) into the incision on the back that was made previously and guide the forceps subcutaneously down the back to the level of the hips [ensure the tips of the hemostats are pointed up, (not towards the spine) to avoid injuring the spinal cord]. At approximately the hip region turn the hemostat tip towards the incision that was made in the leg region and push the tip of the hemostats out of the prepared leg incision.
3. Gently grasp the end of the catheters (**not** the end that will be inserted into the artery/vein) with the forceps and gently pull the catheters through the cavity that was made and ultimately out the neck incision.
4. Place the appropriate blunted-tip needle syringe filled with 20 U/ml Heparin/saline on the end of the respective catheters and fill the catheters (ensure that there are no air bubbles) with the heparinized/saline. Once again check that the catheters are patent and no damage has come to the catheters. Leave the syringes attached to the end of the catheter lines to ensure no air is able to get into the catheter lines and turn the rat onto its back once again.

### 4. Inserting the Catheters into the Femoral Vein and Artery (Figure 3)

1. Place a folded piece of sterile 4.0 silk/thread under the femoral vein and then cut the silk at the folded end. There will now be two pieces of silk under the vein. Or alternatively, place 2 pieces of 4.0 silk under the vein individually.
2. Separate the silk that you placed under the vein, one piece towards the leg (distal end) and the other towards the body. Tie a loose ligature on the side closest to the body, then using small hemostats, grasp the silk and pull taught but do not tighten the knot. Pull the other piece of silk as far as possible towards the leg (distal end) and tie this into a triple knot, grasp the silk with small hemostats and pull taught. This method will allow the vein to fill with blood, making it easier to make the the incision that is required for inserting the catheter (step 4).
3. Place 1-2 drops of lidocaine onto the vein.
4. Using the Vanna micro-dissecting scissors, make a small incision in the vein approximately ¼ thru and at a 45 degree angle.
5. Place fine-tipped forceps (45 forceps) into the incision and using another pair of forceps; carefully feed in the vein catheter. Gently open the forceps that are placed into the vein, as this will allow the researcher to gently place the venous catheter under the forceps and into the vein.
6. When the catheter is fully inserted (approx. 6-7 cm) (when making the catheter a mark is placed on the catheter to assist the surgeon in identifying when the catheter is fully inserted) (this places the venous catheter in the abdominal vena cava), tighten the anterior ligature around the vein and catheter, tying a triple knot (ensure that it isn't occluding the vein). Use the silk suture near the leg (posterior ligature) to again secure the catheter (triple knot) and ensure placement. Slowly draw back the syringe until there is a little blood visible in the catheter, which helps to ensure that the suture knots are not too tight and that the catheter is functional. After checking, depress the plunger until the blood is no longer visible in the catheter.  
Note: it is possible to insert 2 catheters into the femoral vein if needed.
7. Repeat steps 9-13 to place a femoral artery catheter with the following exceptions:
  - a. Tie the silk nearest to the leg (posterior) with a triple knot and pull taught before tying the loose ligature near the body (anterior) prior to making the incision for the catheter placement. This will allow the artery to fill with blood making it easier to cut. Ensure the proximal suture is pulled taught to occlude the artery prior to cutting the artery. This will avoid blood loss when the cut is made.
  - b. Insert the arterial catheter approximately 5 cm from the femoral artery (this places the catheter in the abdominal aorta).
  - c. When securing the catheter with the suture, make sure the suture is not too tight and occluding the catheter.

### 5. Surgical Wrap-up

1. Make a dime to quarter sized loop in the catheters and place on the inside of the leg (the loop should fit in the area that was blunt dissected earlier). After placing both catheters, secure them with 1-2 stitches of 5.0 surgical suture into the muscle layer.
2. Close the incision with 4.0 Ethilon with non-continuous sutures.
3. Turn the rat onto its stomach and make another loop in the catheters about the size of a quarter and place in the pocket dissected in the back. Close the incision with suture.
4. Using a drop of vetbond, secure the catheters in the back.
5. Clamp the catheters near the back incision with padded hemostats and remove the syringes from the ends.

6. Fit the rat with a tether-type jacket, cap the catheters (to maintain the heparin lock), and remove the padded hemostats.

--For long-term maintenance replace catheter saline solution with 20 U/ml heparin/saline.

## 6. Maintenance of Catheter (Sterile gloves should be worn during procedure)

1. Clamp the catheter with padded forceps.
2. Remove the catheter plug.
3. Place a blunt tipped syringe with lock solution onto the catheter.
4. Unclamp the forceps.
5. Fill the catheter with the lock solution (volume is pre-determined-typically 0.3 ml).
6. Clamp the catheter while flushing to prevent any backflow of blood into the catheter tip and remove the syringe.
7. Replace the catheter plug.
8. Unclamp the forceps and gently push the plug in slightly to ensure no blood is in the tip of the catheter.

## 7. Blood Sampling (Sterile gloves should be worn during procedure)

Clamp the catheter with padded forceps.

1. Remove the catheter plug.
2. Slowly withdraw lock solution using a blunt tipped syringe and discard.
3. Attach sampling syringe to the catheter and slowly withdraw the sample.
4. Clamp the catheter with padded forceps and place a syringe with lock solution onto the catheter and re-fill the catheter with the lock solution.
5. Clamp the catheter while re-filling the catheter with the solution.
6. Re-insert the catheter plug.
7. Remove the padded forceps and gently push the plug in slightly further.

## 8. Drug Infusion

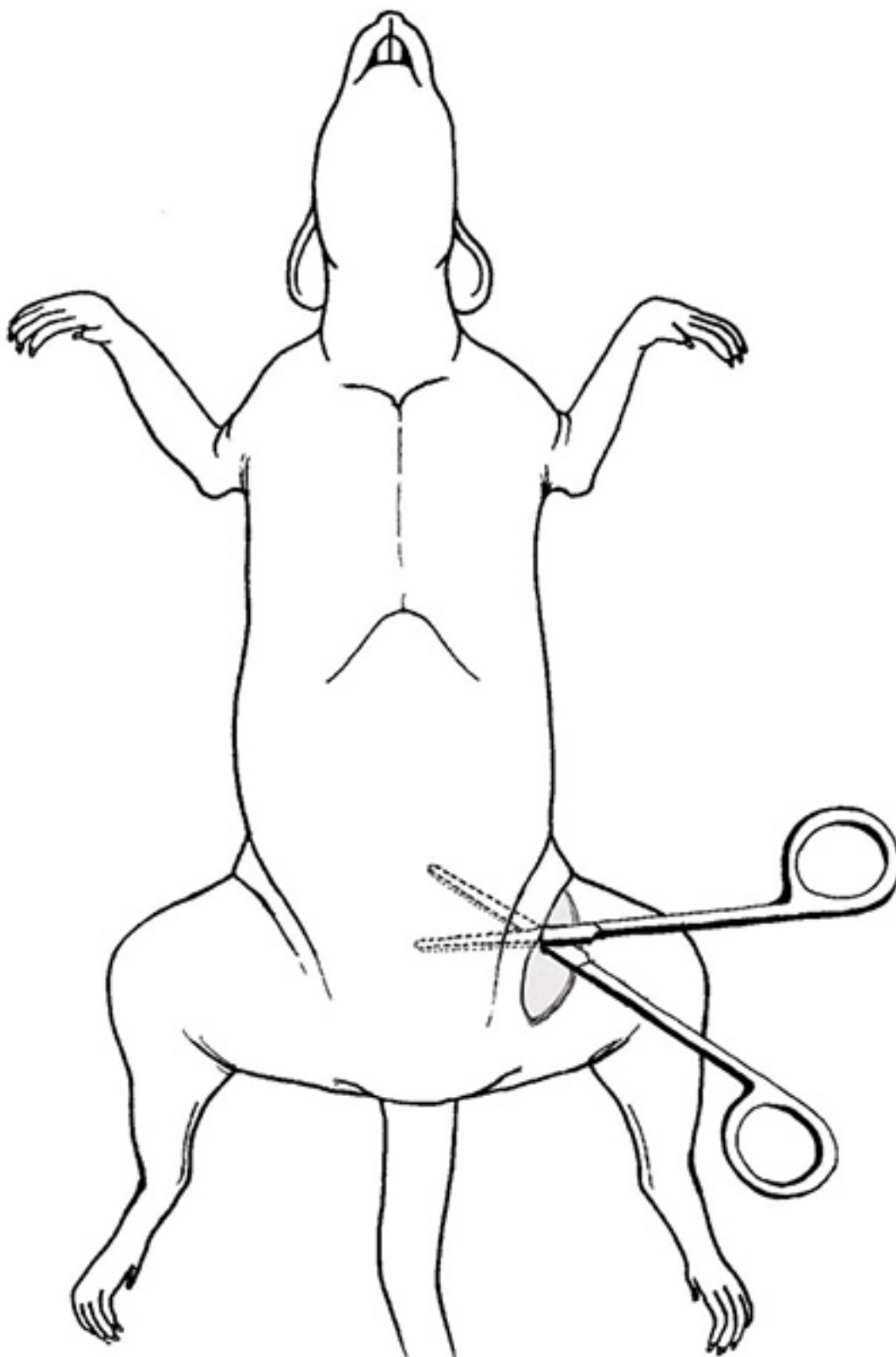
1. Clamp the catheter with padded forceps.
2. Remove the catheter plug.
3. Slowly withdraw lock solution using a blunt tipped syringe and discard.
4. Attach drug filled syringe to the catheter and infuse the substance into the animal.
  - one can use a 3 way stopcock as well as an intermediate if multiple injections are required, thus requiring less fluid infusion into the animal.
  - one can also attach a constant infusion syringe pump with a sterile filter for continuous infusions.
5. Clamp with padded forceps and place a syringe with lock solution onto the catheter and re-fill the catheter with the lock solution.
6. Clamp the catheter while re-filling the catheter with the solution.
7. Re-insert the catheter plug.
8. Remove the padded forceps and gently push the plug in slightly further.

## 9. Blood Pressure and Heart Rate Sampling

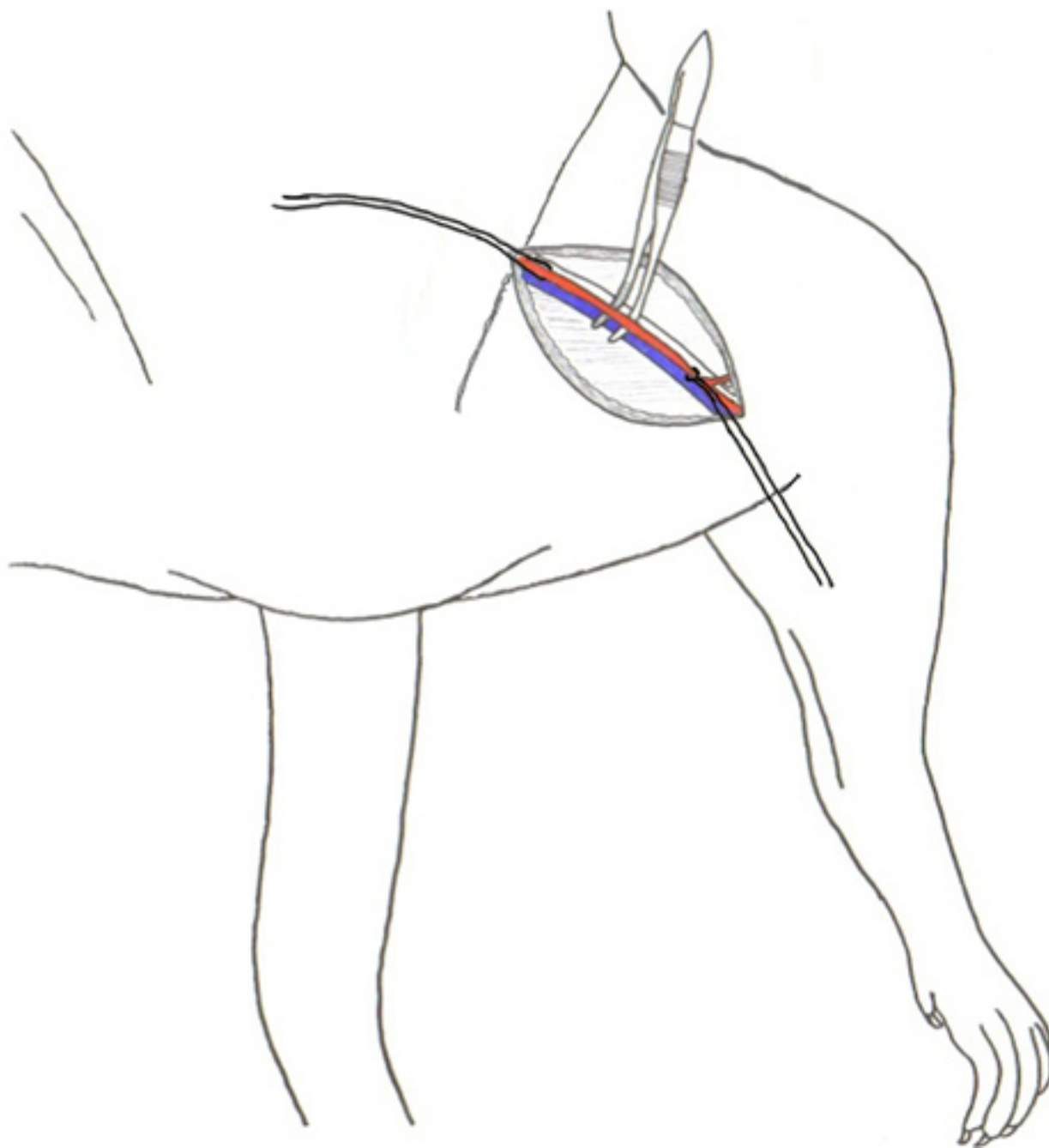
1. Clamp the arterial catheter with padded forceps and remove the catheter plug.
2. Attach the arterial line to the pressure transducer.
3. Follow manufacture instructions for using the software for the blood pressure collection.
4. At the conclusion of the blood pressure monitoring period, using padded forceps clamp the catheter and disconnect from the transducer.
5. Flush the catheter with the lock solution and replace the catheter plug as described above.

## 10. Representative Results

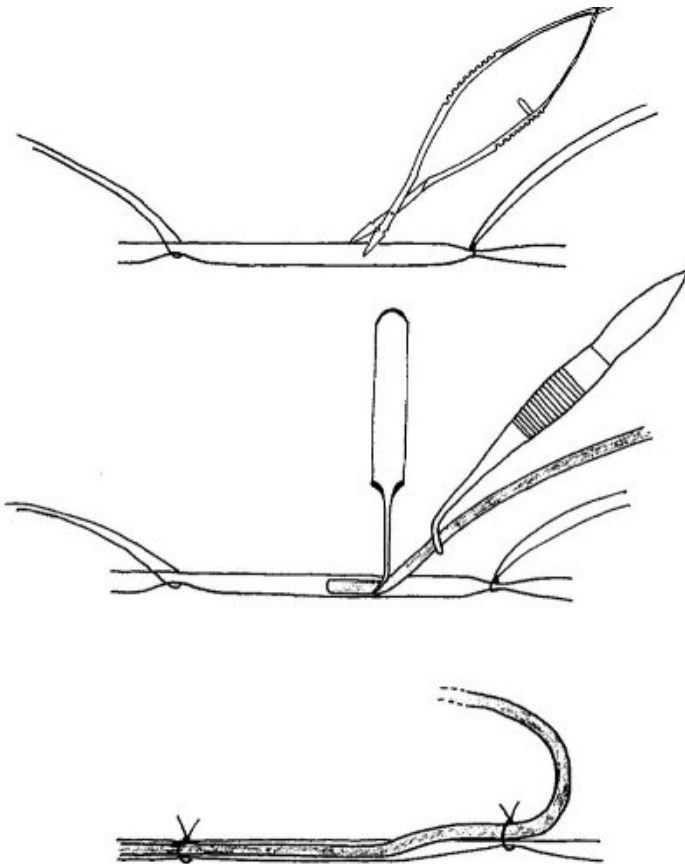
A representative blood pressure measure was taken from a conscious freely moving animal and is presented in Figure 4. Phenylephrine (3 ug/kg, iv), an alpha 1 adrenergic receptor agonist, was administered into the femoral vein line to increase blood pressure, while simultaneously measuring blood pressure from the femoral arterial line. Phentolamine (4 mg/kg, iv), a nonselective alpha-adrenergic antagonist, was then administered to lower blood pressure.



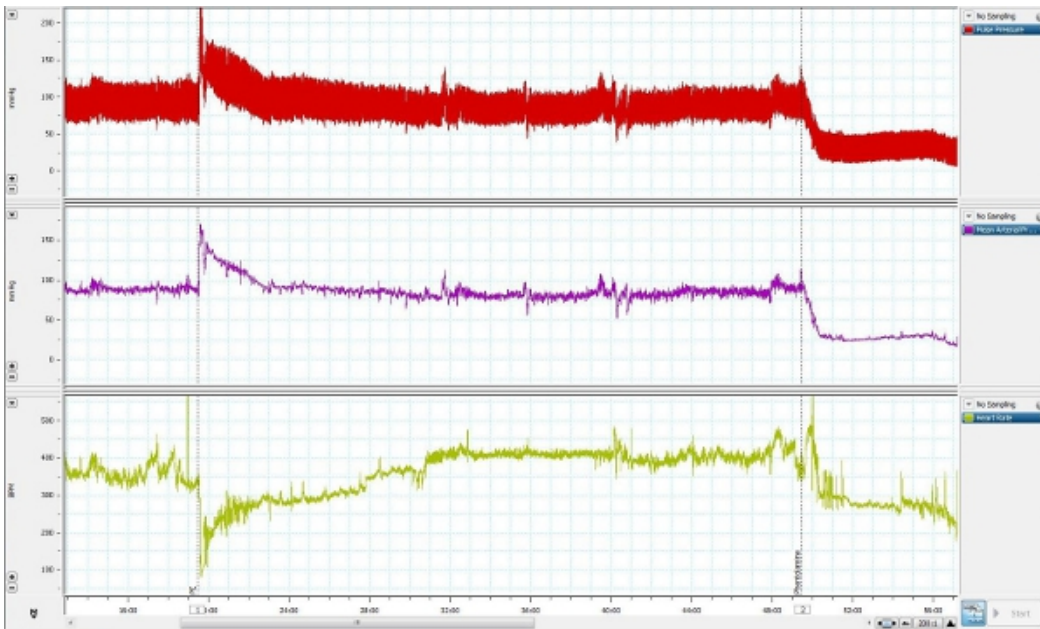
**Figure 1.** Blunt dissection of tissue. With the rat on his back, you will have made approximately a ½ inch (12 mm) incision on the angle of the hind leg and using blunt scissors or hemostats you will bluntly dissect the connective tissue to expose the femoral artery and vein.



**Figure 2.** Separation of femoral artery and vein from connective tissue.



**Figure 3.** Catheter placement. Using Vanna micro-dissecting scissors place a small incision approximately  $\frac{1}{4}$  of the way through the vessel at a 45 degree angle (top) and place fine-tipped forceps into the incision and using another pair of forceps feed the catheter into the vessel (middle). Lastly, upon completion of the placement of the catheter suture the catheter in place (bottom).



**Figure 4.** Representative blood pressure measure taken from a conscious freely moving animal.

## Discussion

Arterial and vein catheterization have historically been used to both acutely and chronically monitor blood pressure, sample blood and deliver substances in the experimental rat animal model<sup>1-4</sup>. A major benefit of these surgical instrumentations is that it allows monitoring procedures,

including, blood sampling, drug administration and blood pressure monitoring, to be conducted with minimal disturbances and/or stress to the animal<sup>1</sup>. Numerous investigators have written protocols and have specific methodologies by which their laboratory performs the surgical procedure<sup>5-8</sup>. The video and illustrations demonstrate what our laboratory has found to be successful with regards to the femoral arterial and venous catheterization procedure.

Rats are commonly used in the laboratory for a multitude of scientific studies due to their small size and convenience in handling. There are several locations where a chronic catheter can be placed within an animal, including the jugular vein, abdominal aorta, carotid artery and femoral artery, to name a few. The rat femoral location for chronic catheterization results in increased length of catheter patency and had the fastest recovery of pre-surgical animal weight compared to other catheter locations<sup>9</sup>.

Numerous investigators have used indwelling catheters for acute as well as chronic blood sampling<sup>1-5,11-13</sup>. In many studies multiple blood draws are required of an animal and external cannulation/catheterization is one methodology that is advantageous due to its non-traumatic nature; moreover it can be done while the animal is conscious, thus is not limited by the effects of anesthetics and also the animal can be freely moving<sup>1,10</sup>. The best method by which to obtain blood samples and to measure stress hormones in rodents has been long debated<sup>6,13</sup>. With regards to pharmacokinetic studies, catheterization of the research animal permits repeated blood sampling with minimal restraint when using a chronically implanted catheter system. In addition, studies have shown reduced basal concentrations of adrenaline, noradrenaline and dopamine in the plasma of freely moving rats (jugular catheter) compared to animals that have been handled (30 seconds) and or restrained (5 minutes)<sup>14</sup>. An additional method by which to discern increases in stress is by measuring plasma corticosterone levels. Previously it was suggested that even following three to four days of surgical recovery times that plasma corticosterone levels were elevated in the chronic cannulated rat<sup>15</sup>. However, recent improvements in methodology have determined that there are no differences in baseline plasma corticosterone levels in the jugular vein cannulated rats compared to uncannulated rats<sup>16</sup>. In addition, HPLC methodology for corticosterone analysis also revealed that corticosterone levels are elevated by restraint stress; however, stable after jugular catheterization<sup>16</sup>.

An additional use of chronic catheterization is the measurement of blood pressure and heart rate in rodents. There are multiple methodologies that are utilized to measure the blood pressure and heart rate in the rat; these include the non-invasive tail cuff methodologies, radiotelemetry procedures and direct indwelling catheters. Each method has its advantages and disadvantages, which are described in detail in other publications. Indwelling fluid-filled catheters can be implanted into multiple arteries within the rat. The femoral artery is but one artery that can be used for this measure. For blood pressure/heart rate measures, the distal end of the catheter is connected to a calibrated pressure transducer. The catheter can be housed in a protective spring that is connected to a swivel to allow free movement of the animal, or attached to a button surgically implanted to the animal. Indwelling catheters have the advantage of minimizing the long-term stress on the animal<sup>17,18</sup>. In addition the materials are inexpensive, calibration is easy for pressure measures and continuous long-term measures can be obtained under conditions of relatively low stress for numerous weeks<sup>19</sup>. We would be remiss if we didn't mention that there are disadvantages to this technique, including, it is a surgically invasive technique, maintenance of the catheter is required to maintain patency, damage to the artery due to the implantation of the catheter and the potential of infection to name a few.

For chronic measures of blood pressure direct recordings from chronically-implanted arterial catheters are more technically challenging but are more accurate and can be done continuously without disturbing the animal. Tail-cuff measurements are less accurate; however they do not require surgery and can also be repeated. Tail-cuff methodologies do require handling as well as heating of the animal to dilate the tail vessels to facilitate the detection of the pulse<sup>20</sup>. Handling and the added heat stress can affect blood pressure measurements, thus not providing truly accurate measures. Moreover, the non-direct tail-cuff method does not permit easy simultaneous blood sampling or drug administration.

An additional method by which direct measure can be achieved is using telemetric methodology. Telemetry allows high-quality recordings of blood pressure (and other measures) continuously for long periods of time in conscious freely moving animals without restraint or anesthetics<sup>18</sup>. However, telemetry devices while ideal are very costly. When compared to telemetry, catheterization benefits include: decreased "setup" and operational costs, the ability to readily administer drugs and easily take blood samples in conscious freely moving animals. The administration of drugs and substances, and obtaining blood samples from the research animal can be done while minimally disturbing the animal, thus minimizing stress to the animal and allowing for a more accurate measure.

## Disclosures

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