

**Osmotic Pump Implantation
In Mice and Rats**
IACUC Standard Procedure
Effective Date: October 2021



Description of procedure:

Osmotic pumps are miniature, infusion pumps which provide researchers with a safe method to deliver agents *in vivo*. The pumps function through an osmotic gradient between the pump and the tissue where the pump is implanted. These minipumps can be implanted subcutaneously, intraperitoneally, intravenously or used for brain infusion. Details may be found on the manufacturer website and/or you may contact the IACUC office.

The following policies must be followed for all implantation procedures:

- UCSF IACUC [Guidelines for Rodent Anesthesia](#)
- UCSF IACUC [Guidelines for Rodent Surgery](#)
- Pumps must be sterile and solutions infused need to be of pharmaceutical grade unless otherwise specified in the protocol.
- Analgesia should be provided at the time of implantation, replacement, and/or explant, per the [LARC Guidelines for Post-Procedural \(Post-Surgical\) Analgesia](#).

The protocol must identify:

- Size of the pump implanted (determine from the size of the animal and manufacture's guidelines)
- The location where the osmotic pump will be implanted
- Solution to be infused (in the agents section)
- How long the pump will be in place (refer to the manufactures guidelines)
- If the pump will be replaced, provide justification and the number of replacements.
- If more than one osmotic pump/animal will be implanted this must be described and justified

Subcutaneous Implantation: The common site for subcutaneous implantation of osmotic pumps in mice and rats is on the dorsum, slightly caudal to the scapulae. Other regions may be used, provided that the pump does not put pressure on vital organs or impede respiration. Absorption of the compound will be through the local capillaries so compounds with slow absorption may require a direct vascular connection.

Subcutaneous Pump Implantation Procedure:

1. Anesthetize and prep the animal following the [UCSF Rodent Anesthesia and Survival Surgery Guidelines](#).
2. Make an incision 1.5 times the diameter of the pump perpendicular to the pump's long axis.
3. Spread the subcutaneous tissue to create a pocket for the pump. The pocket should be large enough to allow some free movement of the pump but not so large that it will slip. The pump should not rest immediately beneath the incision.
4. Insert a filled pump into the pocket, delivery portal first.
5. Close the wound with wound clips or suture.
6. Recover the animal following the UCSF Rodent Anesthesia guidelines and provide analgesia as indicated in the approved protocol.

Intraperitoneal Implantation: Osmotic pumps can be implanted in the intraperitoneal cavity in animals. Allow 24 to 48 hours for the animal to recover after the procedure as feeding and weight gain may be disrupted. For substances which are extensively metabolized by the liver (they have a high “first pass effect”), the intraperitoneal route of administration may produce highly variable concentrations of agent in plasma. Therefore, the intraperitoneal route should be avoided with agents that have a significant “first-pass effect.”

Intraperitoneal Pump Implantation Procedure:

1. Anesthetize and prep the animal following the UCSF Rodent Anesthesia and Survival Surgery Guidelines.
2. Make a 1 cm midline skin incision in the lower abdomen.
3. Tent the musculo-peritoneal layer and incise the peritoneal wall along the linea alba directly beneath the skin incision.
4. Insert a filled pump, delivery portal first, into the peritoneal cavity.
5. Close the musculo-peritoneal layer with absorbable suture taking care to avoid perforation of the underlying bowel.
6. Close the skin incision with wound clips or suture.
7. Recover the animal following the UCSF Rodent Anesthesia guidelines and provide analgesia as indicated in the approved protocol.

Intravenous Infusion via the External Jugular Vein: Using a catheter, pumps may be used to deliver directly into the venous or arterial system. The following procedure details the placement of the catheter in the external jugular vein and requires the attachment of the catheter to the pump. This site is preferable because of its size and ease of access. Alternatively, other sites may be used if described in the protocol.

External Jugular Vein Pump Placement Procedure:

1. Prepare the pump and an appropriate size catheter for placement.
2. Anesthetize and prep the animal following the [UCSF Rodent Anesthesia and Survival Surgery Guidelines](#).
3. Position the animal in dorsal recumbency and elevate the neck to display the ventral neck.
4. Make an incision just lateral to the trachea and dissect down to the external jugular vein so that it can be elevated.
5. Ligate the cephalic end of the vein and place two loose ligatures around the cardiac end of the vein.
6. Insert the catheter into the jugular vein and control hemorrhage with gentle traction on the cephalic suture ends.
7. Tie the cardiac ligatures around the catheter and then tie the cephalic ligature. Trim the ends of all three ligatures close to the knots.
8. Create a pocket on the dorsum of the animal in the midscapular region. Place the pump in this pocket allowing the catheter to reach over the neck to the external jugular vein to permit free head and neck movement.
9. Feed the caudal end of the pump through the tunnel into the pocket.
10. Use a two-layer closure with absorbable material in the underlying fascia and an additional layer of closure for the skin (using wound clips or suture).
11. Recover the animal following the UCSF Rodent Anesthesia guidelines and provide analgesia as described in the approved protocol.

Local Administration of Drugs to the CNS: Direct access to the CNS is useful for testing those agents that affect the CNS but do not cross the blood brain barrier appreciably

Procedure for rats:

1. Anesthetize and prep the animal following the [UCSF Rodent Anesthesia and Survival Surgery Guidelines](#) and then place the animal in a stereotaxic apparatus.
2. A local block is recommended before making the skin incision. Make an incision to expose the skull and remove the periosteal connective tissue.
3. Identify bone suture junctions bregma and lamda to determine and mark the location for cannula placement.
4. Drill a hole in the marked stereotaxically correct location. This hole will receive the cannula.
5. Insert the cannula attached to the pump through the skull and cement in place.
6. Drill a second hole partially through the skull lateral to the cannula to attach a small screw to anchor the cannula taking care not to go through the entire cranium. The screw should extend 1-2 mm above the skull.
7. Dry the skull surface and cover the cannula, implantation site and anchor screw with dental cement or cyanoacrylate adhesive.
8. After the cement has set, prepare a subcutaneous pocket in the midscapular area to receive the osmotic pump.
9. Insert the osmotic pump attached to the catheter leading to the brain cannula into the subcutaneous pocket. The delivery point should be pointed toward the cannula site. The catheter should allow free motion of the animal's head and neck.
10. Close the incision with wound clips or suture.
11. Recover the animal following the UCSF Rodent Anesthesia guidelines and provide analgesia as described in the approved protocol.

For mice: Follow the procedure as detailed for rats with the following exceptions:

- Do not use a stay screw or dental cement as the skull is too thin to support a stay screw.
- The upper portion of the plastic cannula which is used for attachment to the stereotax arm needs to be removed prior to closing the incision.

Targeted Delivery using an osmotic pump

Osmotic pumps can be used to expose a specific, limited region to a compound. Through a catheter introduced into the arterial blood supply to an organ or affixed within or adjacent to the target tissue, the pump provides continuous and controlled input of a compound. A variety of organs and tissues have become target sites for drug delivery using this method, including: arterial wall, mammary gland, muscle, bladder, nerve, bone, ovary, pericardial space, prostate, eye, ear, stomach, testis, kidney, liver, trachea, lymph node, and uterus. Targeted delivery, including target tissue and surgical access, should be described in detail in the protocol.

Explanting Osmotic Pumps

A pump should be removed for the following conditions:

- To verify delivery by measuring residual volume
- To verify stability & bioactivity of the test agent in solution
- No later than the recommended "explant by" date provided by the manufacturer and listed in the protocol
- To replace it with a new pump in order to continue infusion.

Note: IACUC approval is needed if the pump is to be replaced. Also, explanted pumps cannot be re-used.

Explantation Procedure – Survival animals

1. Anesthetize and prep the animal following the UCSF Rodent Anesthesia and Survival Surgery Guidelines.
2. An incision is made in the skin over the area.
3. If the pump has been in place longer than two weeks, or the infusate is an irritant, it may be necessary to free the pump from surrounding connective tissue in order to remove it.
4. Close the incision with wound clips or suture.
5. Recover the animal following the UCSF Rodent Anesthesia guidelines and provide analgesia as indicated in the approved protocol.

Agents: This procedure requires anesthetics and analgesics. All agents administered to animals should be listed in the “Agents” section of RIO.

Adverse Effects to be considered: Infection, dehiscence, skin ulceration, neurological deficits

Resource Consulted:

http://www.alzet.com/products/guide_to_use/implantation_and_explantation.html