rev. 3.01e

Technical Note
Micro SMP-200

Recommendations for Intracerebral Administration

INTRODUCTION

iPRECIO® is a completely implantable, programmable micro-infusion pump system for experimentation in small laboratory animals. The pump has a built-in microprocessor which can be programmed to administer small volumes, in vivo, for extended durations. Additionally, the pump houses a septum designed for percutaneous access, through which filling and exchange of solutions is made possible. The iPRECIO® system's highly precise, in vivo-, capabilities uses a patented, high accuracy, mechanical pump technology, the "Rotary Finger Method", which was developed by Primetech.

Intracerebral administration is the only way to deliver a drugs directly into the cerebral ventricle (intraventricular) or cerebral parenchyma (intraparenchymal) without crossing the Blood Brain Barrier. This ability to infuse directly into the brain with a specialized infusion kit in combination with a programmable and refillable implantable pump makes it an ideal behavioral pharmacological model where stress is significantly reduced in a freely moving animal. Very sensitive acute and chronic studies may be achieved with this iPRECIO® and brain infusion kit combination.

This technical note assumes prior knowledge and expertise on the use of stereotaxic atlases and stereotaxic apparatus to design and locate the appropriate infusion sites within the brain. Therefore, desired depth below Plastic Pedestal of Cannula must be calculated along with appropriate stereotaxic coordinates for the target infusion site. Prior knowledge of identifying bone suture junctions, bregma and lambda is also expected. Surgery experience required for this operation is also assumed.

WARNING：iPRECIO® Micro – Infusion Pump is not intended for human use.

REQUIREMENTS

Perioperative Care

- Antibiotics and the treatments
- Anesthetic agents and the techniques
- Heating Pad
- Surgical glove, mask, cap and gown
- Sterilized gauze
- 70% Isopropyl alcohol
- Disinfectant soap
- Sterile saline
- Electric shaver or Hair remover

Pocket and Tunnel Making

- Surgical scissors, tweezers, forceps, and sterile scalpel blade with handle

Pump Fixation

- 3-0 to 5-0 non-absorbable suture with curved needle

Brain Infusion Cannula Fixation

- Brain infusion cannula (OP cannula supplied by Plastics One, with a choice of depth and gauge size below pedestal.)
- Stereotaxic apparatus and micromanipulator with mounting holders (Brand Specific Mounting holders supplied by PlasticsOne)
- Microscope
- Surgical retractor
- Micro drill (D#56 for anchor screws and D#69 for 22 gauge skull penetration supplied by Plastics One)
- Stainless steel anchor screw (0-80x1/16 with 1.6mm thread length or 0-80x3/32 with 2.4mm thread length supplied by Plastics One)
- Screwdriver (Screwdriver supplied by Plastics One, PART No. SD-1)
- Dental cement (300CAGS medical grade Cyanoacrylate gel, 3g tube, supplied by Plastics One)

Wound Closing

- Wound clips and wound clips applier
- Tissue adhesive (3M™ Vetbond™ Tissue Adhesive supplied by 3M)

METHODS

1. Perioperative Care

Careful attention to sterile techniques and the use of sterile equipment are crucial to successful surgery. Additionally, antibiotics are most effective to administer pre- and post-surgery in order to maximize blood levels during surgery and recovery. Primetech recommends the use of a heating pad to prevent decreased body temperature in the peri- and post-operative animal.

2. Anesthetize the Animal

Anesthesia must be used to ensure a reliable experimental result. General anesthesia should be maintained for around 20 – 30 minutes. Primetech recommends using an anesthetic method that supports prompt post-operative recovery like isoflurane.

3. Brain Infusion Cannula Attachment ⋯See Fig.1

1. Cut the outlet tube around 10cm under sterile conditions.
2. Connect the outlet tube to the brain infusion cannula.
3. Fill the solution to the cannula tip.
4. Activate the pump.

4. Pocket Making ⋯See Fig.2

1. Position the animal in sternal recumbency on the heating pad.
2. Remove the hair from incision site and scrub with disinfectant soap and isopropyl alcohol. A series of three scrubs with both the disinfectant soap and alcohol is recommended.
3. Make a 6cm midline incision through the skin from the posterior margin of the eyes to a point midway between the thoracic vertebrae. Start with a scalpel on the skull section to the make this midline incision and then continue to cut the skin with scissors on the vertebrae.
4. Using blunt dissection, create a pouch under the skin from the point of the incision to the caudal area by separating the skin from the underlying tissue with scissors or forceps.

The pocket should be the appropriate size (not too large and not too small) for pump fixation, low-stress implantation for a successful long-term infusion.

5. Pump Fixation ⋯See Fig.3

1. Place in the pump into the pocket.
2. Suture the pump through the muscle layer.

Over tightening of the sutures may induce a tissue necrosis and laceration due to compression.

6. Access to brain ventricle ⋯See Fig.4

1. Position the animal in a stereotaxic apparatus in sternal recumbency.
2. Retract the skin at parietal region of the incision using a retractor.
3. Wipe away the skull of tissue down to the bone using sterilized gauze.
4. Using a micro drill in a circular motion under the microscope, make an anchor hole in skull at the desired location. The hole should not penetrate the skull but should be deep enough for the anchor screw.
5. Attach an anchor screw.
6. Using a micro drill in a circular motion under the microscope, make a 1mm diameter hole in skull at the desired location. When drilling, a thin layer of bone should be kept at the bottom of hole.
7. Remove the thin bone layer with tweezers.
8. Insert the cannula connected the micromanipulator into the cerebral ventricular.
9. Thoroughly dry the skull surface site and apply dental cement to the cannula pedestal, the anchor screw, and surrounding bone.
10. Once the dental cement is set, release the micromanipulator and the retractor.
11. Cut a break-off segment with a nipper.
12. Cover the remaining pedestal by applying additional dental cement.

7. Wound Closing

1. Close the skin incision with non-absorbable suture or wound clips. Once closed, seal the incision with tissue adhesive.

Proper pocket closing will help in wound healing and help to prevent infection. Apply iodine on sutured skin to reduce risk of infection.

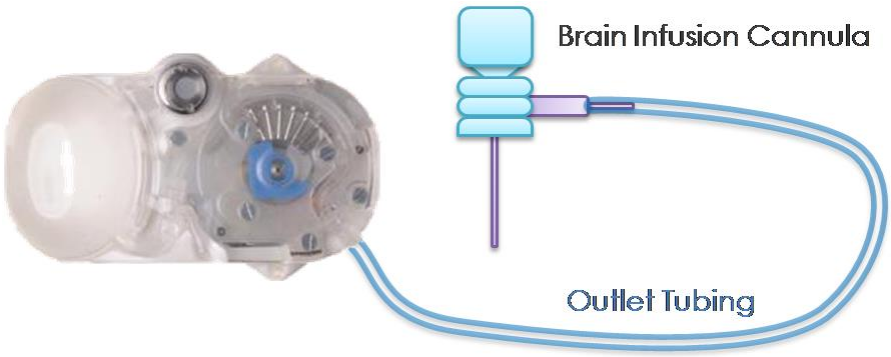

Fig. 1 Connect the brain infusion cannula

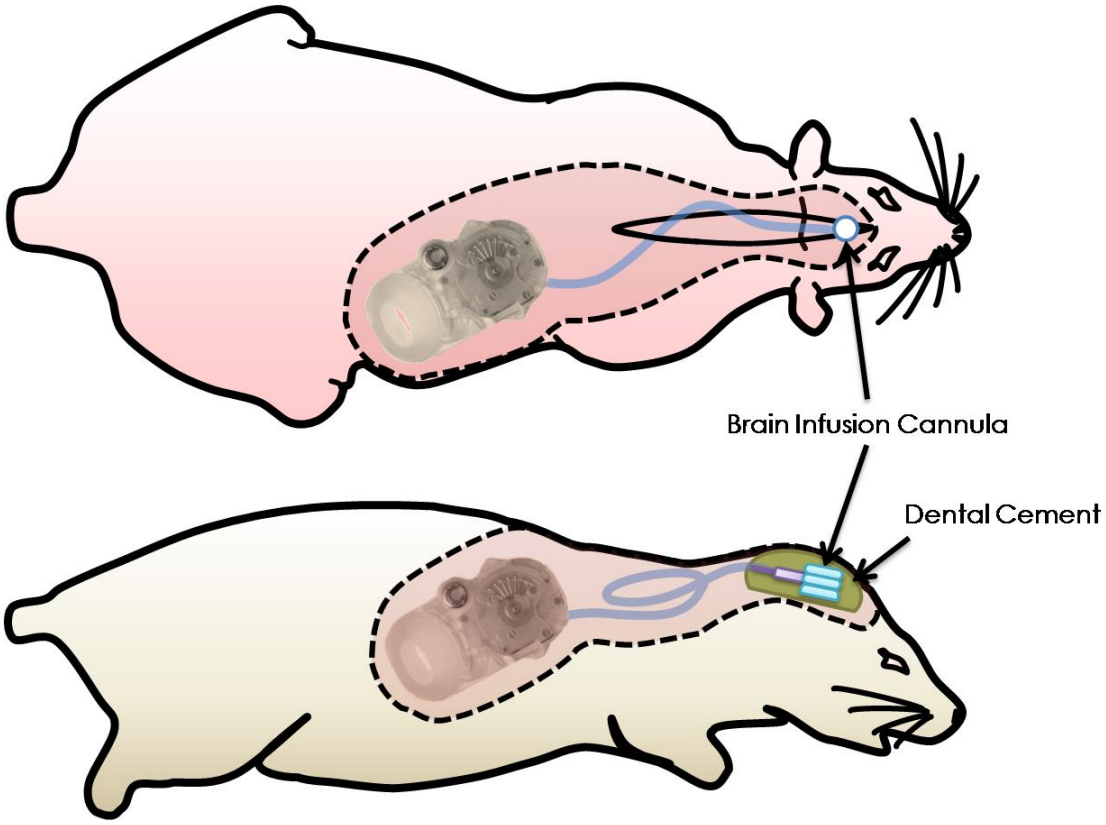

Fig. 2 Dimensional drawing of the pump pocket and the cannula placement

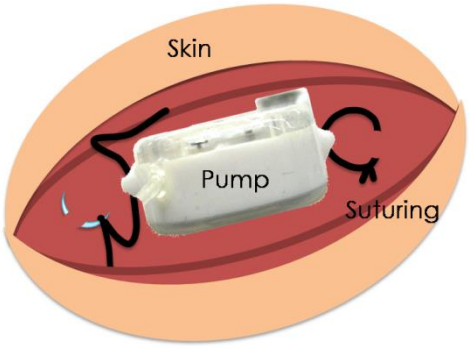

Fig. 3 Pump Fixation: View from the back of the pump with septum port on the right hand side

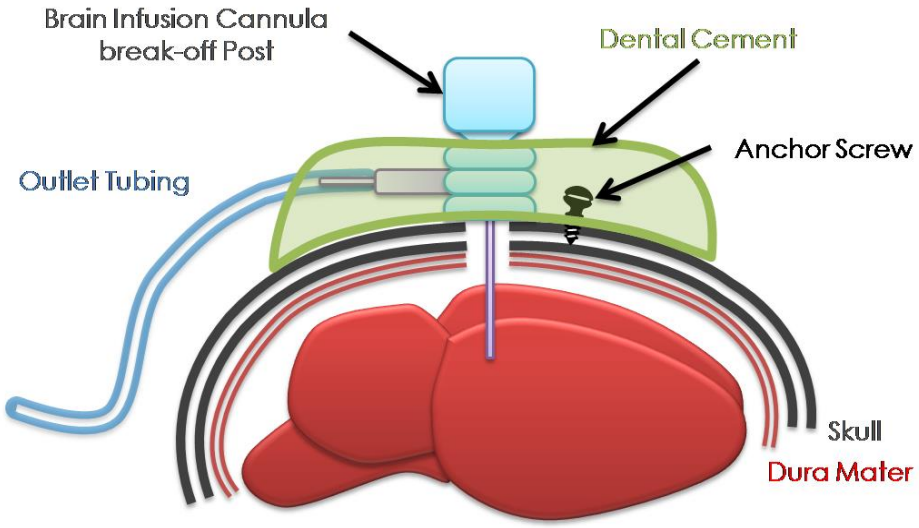

Fig. 4 Brain infusion cannula placement.

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PlasticsOne® A medical Component Manufacturer. Phone +1-540-772-1166 Fax +1-540-989-7519
http://www.plastics1.com/PCR/Preclinical-Research-Components.php

322OP/Starter Kit — Cranial Infusion Kit for iPRECIO® Pump

322OP Subcutaneous Pump Cannula, 22gauge	(5)
0-80x stainless steel anchor screws	(5)
MH-300 Manipulator Mounting Holder	(1)
300CAGS Cranial Cement, 3 grams	(1)
DH-1 Drill Bit Holder	(1)
D-69 Bit, for 22 gauge Skull Penetration	(1)
D-56 Bit, for 0-80x stainless steel anchor screws	(1)
SD-1 Screw Driver	(1)

Please provide the following information:

1. __ mm Depth below Plastic Pedestal of Cannula
2. _____, Brand Name of Manipulator
3. Mark choice of 1/16 or 3/32 stainless steel screw

322OP/Kit

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