Refinement of Vascular Catheterisation in Rats: Use and patency of PinPort™

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1 INTRODUCTION

Placement of vascular catheter facilitates blood withdrawal and/or administration of compounds in animal models. It is considered a refinement to frequent handling and repeated vascular punctures. Under general anaesthesia, vascular catheters are surgically placed inside a vein or artery and exteriorised to enable easy access. The exteriorised portion of the catheter is typically connected to a syringe or, through an extension, to sampling or infusion equipment.

We have explored if the catheter connection of the exteriorised portion can be enhanced and patency extended with the use of an external access port, i.e. PinPort™(Instech Laboratories, Inc., USA) - (Figures 1 and 2), and conducted an initial pilot (n=12) and subsequent validation study (n=12) in CD®IGS rats. Under general anaesthesia, vascular catheters are surgically placed inside a femoral vein and exteriorised to enable easy access.

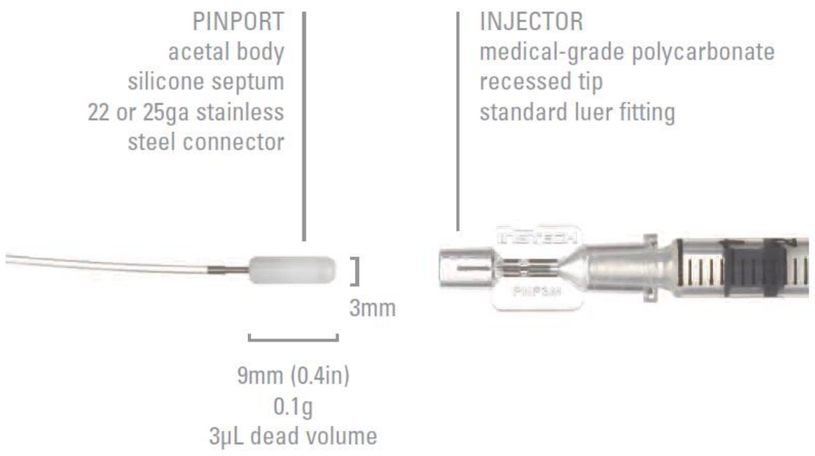

Figure 1: PinPort™ and injector

2 MATERIAL

Rats CD®IGS (SD) 250-275g male from Charles River Laboratories, France were used in this study. Rats originate from a barrier facility with SPF/VAF Plus health status, as defined by Charles River Laboratories. Rats were housed in open top cages, fed irradiated pelleted VRF1 diet (SDS, UK). They were housed on autoclaved aspen BK 8-15 (J. Rettenmaier & Sohne GMBH) bedding with Enviro-dri ® nesting material for enrichment (SERLAB, France). Rats had filtered water (0.1 µm) provided *ad libitum*.

Following pre-operative acclimatisation and assessment rats were anaesthetised with intra-peritoneal (IP) injection of ketamine (Imalgene, Merial, France) 43mg/kg and xylazine (Rompun, Bayer, France) 8.7mg/kg. Vascular polyurethane catheters were implanted using aseptic surgical techniques, through a femoral vein with catheter tip positioned within the abdominal portion of the *vena cava*. The vascular end of the catheter was secured in place whilst the other end was tunneled through subcutaneous fascia and exteriorized in the inter-scapular region.

The polyurethane catheter was secured to the skin in the inter-scapular region using a non-absorbable suture, prolene 4-0 (Ethibond). The PinPort™ was connected to exteriorized part of the catheter and fixed securely with a drop of Loctite® (Henkel) glue

Anaesthesia was reversed with subcutaneous (SC) injection of atipamezole (Antisedan, Orion pharma, UK). Peri-operative analgesia was provided with buprenorphine (Buprecare ®, Axience S.A.S.) 0.05mg/kg SC on day of surgery, and day 1 post-op. Additional doses were provided as required.

Catheters were flushed with sterile and apyrogenic saline solution (NaCl 0.9%, B.Braun) and locked with heparin (500USP/ml) glycerol Cath-LocHGSH (High Viscosity, SAI Infusion Technologies, USA).

Rats were housed individually in surgical facility accredited by the French Ministry and AAALAC International.

3 METHODS

1) Study to assess patency with low usage

The catheters were flushed starting at day 5 after surgery, then every day until the patency was lost. Flushing was performed using aseptic technique. First the heparin glycerol lock was extracted, the residual blood present inside the catheter was flushed using 0.3 ml of NaCl 0.9%, and finally, the heparin glycerol lock was replaced.

2) Study to assess patency with intensive usage

The attachment in the inter scapular region was supported by an additional non-absorbable suture around the catheter, between the PinPort™ and the retention bead. Catheters were flushed 3 times a day starting from Day 4 after surgery, for a 15 consecutive days, except during weekends. Flushing technique was identical to low usage study with the exception that the following morning and midday sampling, the catheter was not locked with heparin glycerol, but filled with NaCl 0.9%. The heparin glycerol lock was replaced after the evening sampling.

All animals with functional catheters (fully patent) were euthanised on day 37 (1st study) or day 18 (2nd study) and assessed macroscopically for the presence of signs of infection or inflammation.

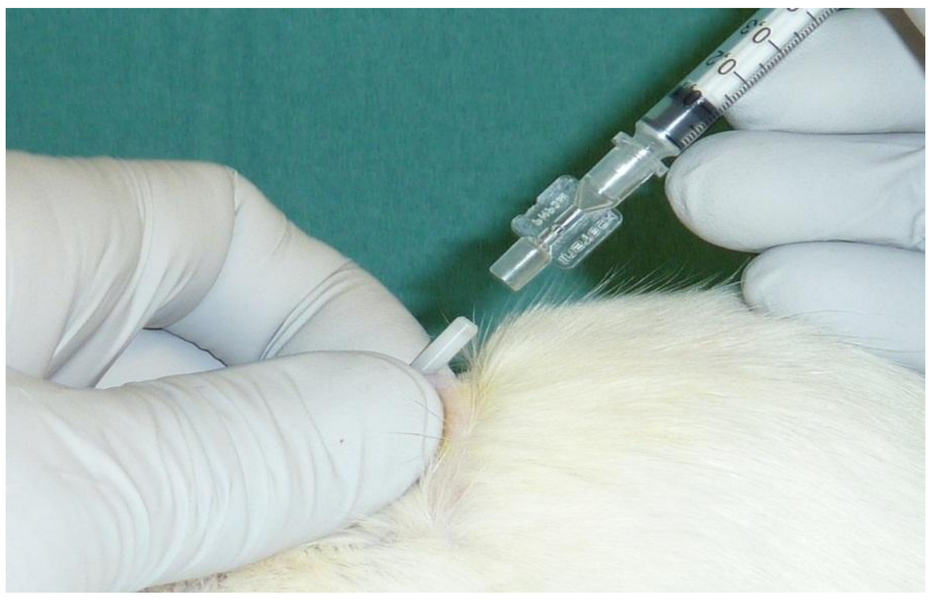

Figure 2: Rat fitted with a PinPort™

4 RESULTS AND CONCLUSIONS

In the low usage study 9/12 rats (75%) remained patent throughout the 37 days of the study. 3 rats were euthanised due to detachment of the catheter in the inter-scapular region.

In the intensive usage study 12/12 rats (100%) remained patent throughout the 15 days of intense usage. Evening sampling was more challenging and required extra flushing to remove blockage. This was attributed to the absence of glycerol heparin lock-solution that wasn't replaced the following morning and midday flushing.

We conclude that PinPort™ can remain in place for up to 30 days (low usage) and with a guaranteed vascular catheter patency for up to 15 days, if associated with intensive usage.

No adverse effects were observed in animals during the study and post-mortem abnormalities were not observed.

We are continuing to refine this model and gathering additional data. We believe that PinPort™ can extend the catheter patency and minimise catheter related complications if aseptic techniques and adequate lock and flushing solutions are used.