

Implantation of Rat Vascular Access Buttons in GÖTTINGEN MINIPIGS

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Introduction:

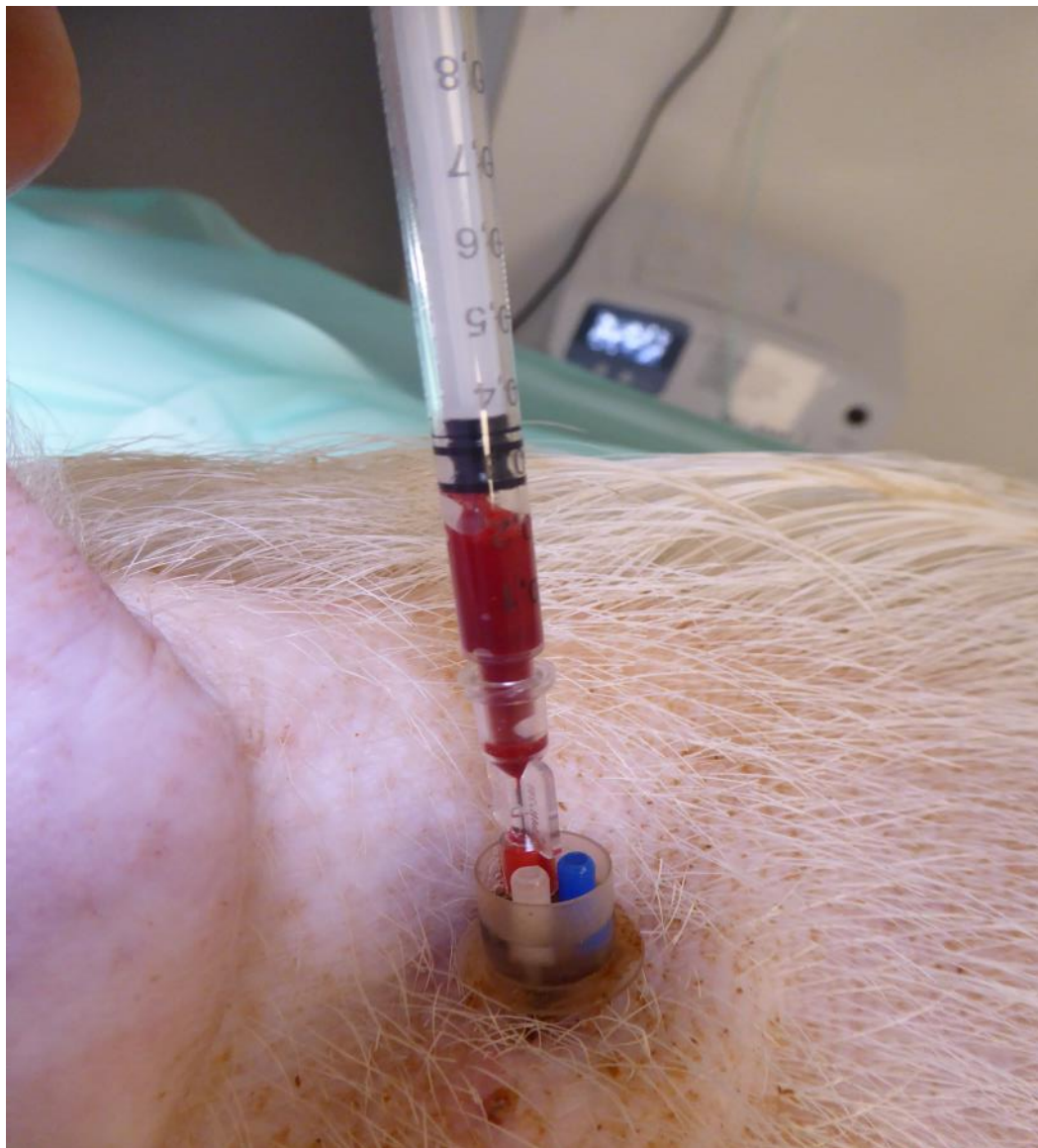
Infusion and serial blood sampling are often important technical aspects of an experimental design. Superficial vessels in the minipig are few and frequently accessing them is a challenge. Although minipigs have a convenient size for handling, restraint and venepuncture can be stressful and affect blood parameters. Therefore, when experiments require infusion or frequent blood sampling, catheterization is often the best option, both ethically and scientifically. The implantation of Vascular Access ports and Seldinger Catheters is described and published in various variations. To add another option when choosing the optimal study design, we tested the Rat Vascular Access Button™ in Göttingen Minipigs. The button allows up to three catheters to be connected and opens the possibility to sample and dose via one device but trough different catheters. This has, to our knowledge, not been done before.



Minipig in pen after surgery



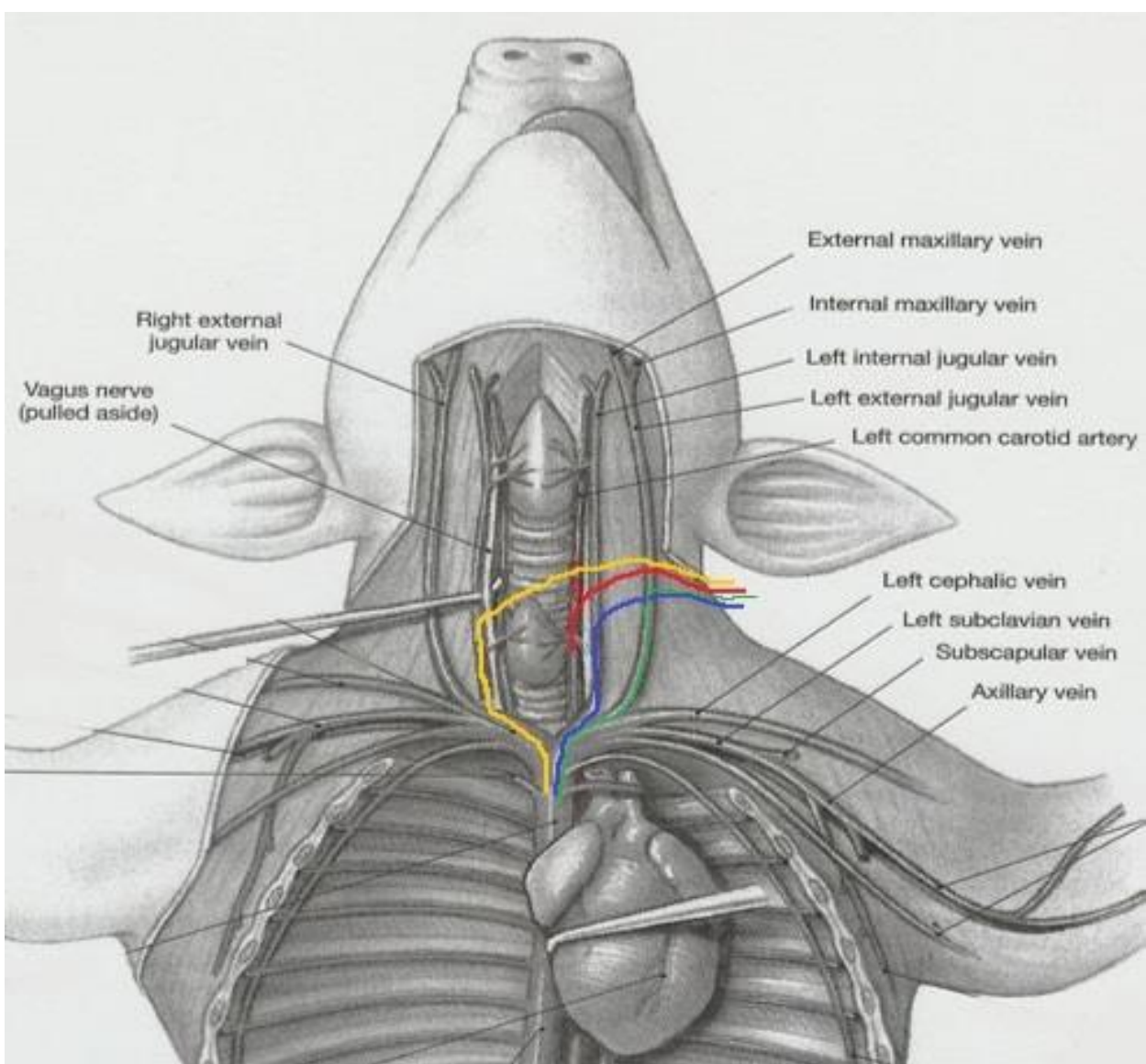
Button implanted behind the ear



Taking a blood sample



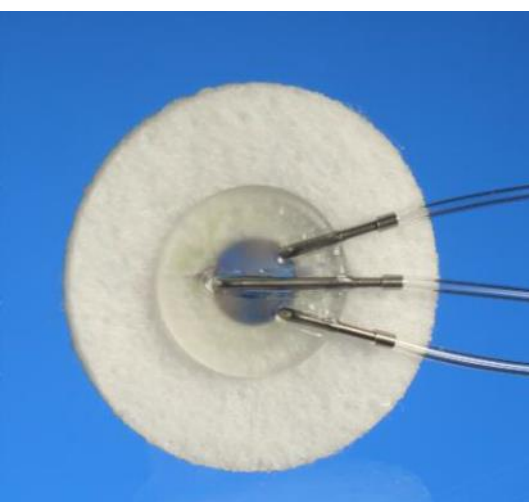
Blood sampling performed by one person with Minipig in a sling



Placement of catheters, colours explained in text below



Rat Vascular Access Button ready to im-plant. (above)



VAB after 2 months at necropsy. Dracon cuff is completely ingrown in the sur-rounding tissue. (right)



Material and Methods:

Three studies were conducted:

1. Pilot

Proof of concept, determine best approach and type of catheter.

4 male Göttingen Minipigs (14 -15 kg). Rat Vascular Access Buttons (Instech Laboratories, Inc. USA) with three ports for three catheters. Each Minipig had three catheters implanted from a midline incision:

- In the left carotid artery; two Minipigs in cranial direction and in two in caudal direction. A 3fr PU catheter, with a bead at 3 cm was inserted to that length and fixed with a purse string suture and tissue glue. (red)
- In the left internal Jugular vein. This vessel runs alongside the carotid artery. It was ligated and a 3fr PU catheter, with two lateral perfusion holes, at 3 cm and 2 mm apart was inserted to a length of 7-8 cm, so the tip rested in the vena cava. (blue)
- In the right internal jugular vein. A 3fr PU catheter, was inserted in the same manner as in the other vein. (yellow)

2. Housing

Feasibility test of Group housing

4 male Göttingen Minipigs (17 –20 kg). Rat Vascular Access Buttons (Instech Laboratories, Inc. USA) with one port, no catheter implanted.

Some caps were camouflaged with a less obvious colour and some had a bit-ter tasting additive. It seemed to make no difference. If caps fell of it was mainly due to lack of magnetic adhesion or intensive movement.

3. Main study

Increased animal number applying results from pilot. (ongoing)

16 Göttingen Minipigs (10 –12 kg). 8 males , 8 females. 8 with Rat Vascular Access Buttons of one port/catheter, 8 with Buttons of two ports/catheter.

The left external Jugular vein was dissected and after ligation one ore two 3fr PU catheters were 7 cm inserted. If there was two catheter the insertion was trough the same puncture and insertion length was 7 and 9 cm. Catheters were secured around the vessel with a modified Miller knot, followed by square knots. Another tie crani-al of the bead was placed an the catheter was further secured with the ends of the initial ligature. Incision closed in three layers using PDS II, continuous pattern, the last intradermal. (green)

All catheters were tunnelled to a subcutaneous pocket created behind the left ear and then connected to the button. The incision of the implantation site was closed in three layers, anaesthesia discontinued and the minipigs left to recover. After one week of post op care, including antibiotics and analgesia, vascular access was tested. In the group housing study the animals were euthanized after that period. For a period of two or three months the buttons were accessed roughly every 7 days to test patency and functionality. At the end of that period the animals were sacrificed, and a necropsy of the affected area performed.

Results:

The incisions in the neck and at the site of the button healed really well and no signs of infection or other complications were observed. The felt collar of the button was grown in the subcutaneous tissue to seal the exit site completely.

All ports worked fine, but some typical catheter related issues appeared after some time. The table below shows clearly that the standard catheter in the vein worked best.

Catheter issues withdraw			Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
Catheter 1 Artery	Cranial	A		S	R	B	B	B	B	B
	Cranial	B			S	R	R	R	R	R
	Caudal	C			R	R	R	R	R	R
	Caudal	D		R	R	R	R	R		
Catheter 2 Perfusion holes	A			S	B	B	B	B	S/B	B
	B		S	S	S	R	B	S	S	R
	C			R	B	B	R	R	B	B
	D			R	R		R	B		S
Catheter 3 Standard	A							R	R	
	B									
	C									R
	D					S				

Results of 8 weeks testing. S= slow withdraw; R= fine after rinsing; B=blocked even after rinsing

Conclusion and Discussion:

It can be concluded that Rat Vascular Access Buttons™ can successfully be implanted in Minipigs and provide long term vascular access. The buttons can accommodate 1-3 catheters which gives the opportunity to infuse and sample trough the same unit without cross-contamination. Implantation is a permanent procedure; catheters can be explanted but this is not possible for the VAB as it is ingrown.

Infection around the VAB can possibly be reduced by making sure the Dracon cuff rests between the muscle and the fat layer and the skin is snug around the neck of the VAB.

Accessing is painless and if the Minipigs are trained to be in a sling, only one person is required to perform procedures.

There are typical catheter related issues, that can be minimized by proper catheter handling, namely locking under positive pressure.

Preliminary results of the main study show, that the assumed advantage of having two catheters (having a backup if one is blocked) is not necessary true. Blocked catheters can become patent again after some time or repositioning the animal.

All procedures were carried out in compliance with current laboratory guidelines for good conduct and the project was conducted with approval of the Danish Animal Experiments Inspectorate according to Danish law. Animals were housed at approved facilities, and taken care of by qualified persons.

In the main study the incisions in the neck and at the site of the button healed well and no signs of infection were initially observed.

Four weeks post surgery we found some infections around the button in 6 cases, 3 of them were minor and disappeared quickly after treating with antibiotics. One remained a bit longer and two animals were euthanized (5 and 6 weeks after surgery) as the button was no longer embedded thoroughly in the tissue.

Necropsy showed that the infection was limited around the button with a folded up Dracon cuff. It might have been due to improper implantation in the fat rather than below the fat layer. The tip of the catheter was where it was supposed to be, in the vena cava and no signs of clots or thrombi were observed.

In some cases function of both catheter stopped at the same time.



Artery Perfusion Standard

Rinsed Catheter tips at end of the pilot study. All catheter with perfusion holes had large fibrin deposit, whereas standard ones were clean. Artery catheters had some fibrin attached.

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