Refinements of Jugular Vein Catheterization with Vascular Access Button in Mice

Lapierre A, LaFleur R, Kane K, Lyons B
The Jackson Laboratory, Bar Harbor, Maine/Sacramento, California

ABSTRACT
Mice implanted with a jugular vein catheter with a vascular access button (VAB) are used extensively in research for studies requiring repeated infusions over time. Multiple designs of VABs for use in rodents are available but most were originally developed for rats and therefore not optimized for use in the mouse. We found, across multiple strains of mice, that the use of a VAB with a polyester felt disk elicited a strong inflammatory reaction with poor wound healing and pressure necrosis due to the composition and stiffness of the disk. To increase the biocompatibility of the VAB disk, we designed a silicone mesh disk in collaboration with the manufacturer. The disk is perforated medical-grade silicone which provides greater flexibility to mold to the body contour and enables tissue ingrowth through the perforations for optimal healing. Initial studies were conducted using the silicone disk. The silicone disk was well tolerated with normal wound healing without evidence of pressure necrosis. A further refinement was to exteriorize the VAB through a circular incision made with a skin punch rather than through a traditional linear incision. This technique was performed (n=70) and the circular incision eliminated the need for skin sutures and maintained the VAB in position on the dorsal midline. These refinements align with the 3Rs by optimizing wound healing and improving animal welfare.

INTRODUCTION
Our initial studies in mice using a commercially available vascular access button (VAB) resulted in injury to the overlying tissue. We found, across multiple strains of mice, that the use of a VAB with a polyester felt disk elicited a strong inflammatory reaction with poor wound healing and necrosis due to the composition and stiffness of the disk. In order to minimize the tissue reaction caused by the composition of the VAB disk (Figure 1), we explored the use of an alternative material. Silicone was selected due to its high biocompatibility and flexibility. To integrate the VAB with the overlying skin, perforations were added to the disk to allow tissue ingrowth. In collaboration with the manufacturer, various designs were developed and evaluated at our facility (Figure 2).

METHODS
VABs with a 14 mm diameter silicone disk containing either 4 or 8 perforations of 1 or 2 mm diameter were implanted in 8 week old C57BL/6J male mice. As a further refinement, we employed a circular incision to exteriorize the VAB in the interscapular region, instead of the conventional linear skin incision. The skin was folded and a punch was used to create a half circle through the 2 layers of the folded skin (Figure 3) resulting in a complete circular incision. The silicone disk was folded to facilitate the VAB insertion via the ventral neck incision and to ease subcutaneous tunneling to the circular incision. The port was exteriorized using forceps and the silicone disk flattened in place (Figure 4).

FIGURES


Figure 1: Tissue reaction elicited by the felt disk

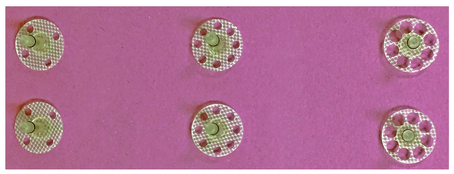

Figure 2: Different silicone disk prototypes

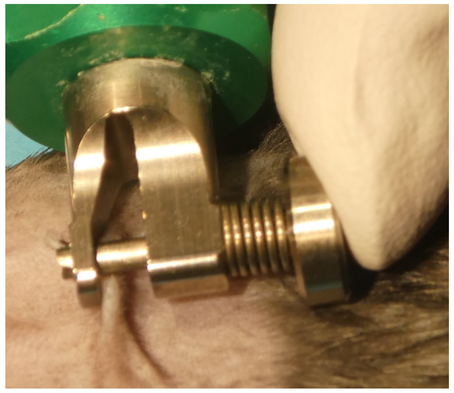

Figure 3: Skin is folded and a half circle skin punch is performed to create a circular incision

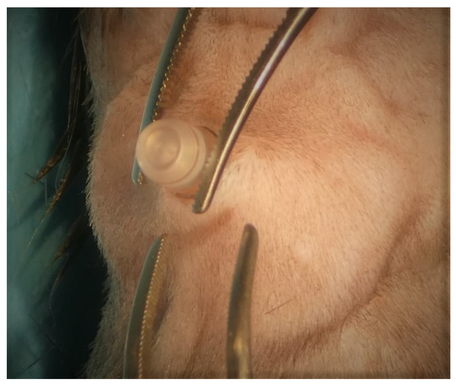

Figure 4: Exteriorized VAB in interscapular region

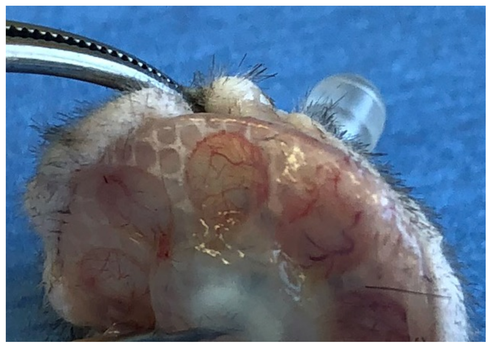

Figure 5: Ingrowth of tissue through the disk perforations

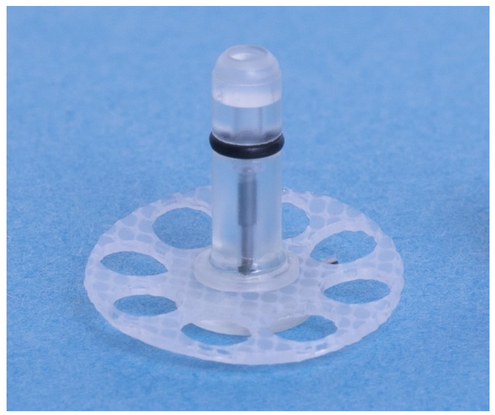

Figure 6: The silicone disk VAB with 8, 2mm perforations currently used at our facility

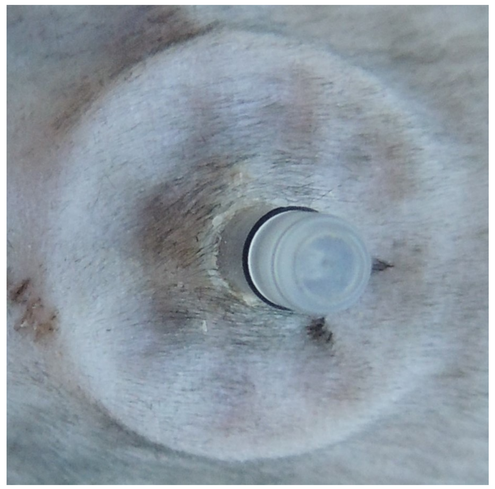

Figure 7: Tissue necrosis is absent with the silicone disk

1. Wei, J.C.J., Edwards, G.A., Martin, D.J. et al. Allometric scaling of skin thickness, elasticity, viscoelasticity to mass for micro-medical device translation: from mice, rats, rabbits, pigs to humans. Sci Rep 7, 15885 (2017).

METHODS - CONTINUED
The dorsal skin incision did not require suture for closure as the circular incision closely fit the port. A study was conducted in (n=70) 8-week-old C57BL/6J male mice. Mice were monitored for wound healing, skin reaction to the VAB and catheter patency.

RESULTS
Gross examination of the disk/subcutaneous interface demonstrated ingrowth of tissue through the disk perforations (Figure 5). The disk with eight 2 mm perforations maximized tissue ingrowth while maintaining the integrity of the disk (Figure 6). The silicone disk was well tolerated and tissue necrosis was not present in any of the mice (Figure 7). The circular incision site created by the punch maintained the VAB in position without the use of skin sutures.

DISCUSSION
Differences in skin thickness and viscoelasticity[1] likely contributed to the lower tolerability, in mice, to the polyester felt material in conventional VABs. Because silicone has a more favorable biocompatibility than polyester, we hypothesized that replacing the polyester material with silicone would improve the tolerability of the VAB in mice. We found the use of silicone moderated the inflammatory reaction of the tissue and its flexibility eliminated the associated necrosis. To reduce the amount of foreign material needed to close the skin, we used a circular incision to exteriorize the port of the VAB in place of a linear incision that would require suture material.

CONCLUSION
Implementation of these changes improved the welfare of the mice and reduced surgical time. We are committed to the 3Rs and strive to enhance animal welfare by refinement of surgical techniques.

ACKNOWLEDGMENT
We would like to acknowledge our dedicated surgical team for their participation in performing the surgical procedures.

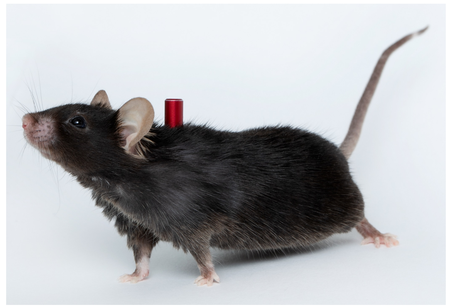

Figure 8: A 78 week old C57BL/6J male with a silicone disk VAB with a protective cap

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