Investigation of large volumes and high flow rates in subcutaneous dosing in Göttingen Minipigs

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AIM

The Göttingen Minipig was investigated as a model for subcutaneous injection with large volumes and fast flow rates. The test variables were injection location (neck, dorsal and ventral flank), volume (15 and 50ml), and flow rate (15, 30 and 50 ml/min). Three locations on the animal was tested; Neck, dorsal and ventral flank. Two volumes and three flow rates were tested.

Volume (ml)	Flow rate (ml/min)	Time (mm:ss)	Neck (success/total)	Dorsal flank (success/total)	Ventral flank (success/total)
50	5	10:00	5/9	7/8	5/6
15	15	01:00	7/13	9/16	10/14
15	30	00:30	2/8	4/6	6/12

METHOD AND MATERIALS

Animals: 9 male and 4 female Göttingen Minipigs, 6-7 months of age, weighing 11,3-16,4 kg. Animals were kept anesthetized during the study for up to 3 hours with a Zoletil mixture. The animals were placed on pads heated to 37 degrees Celsius. At the end of the study, the animals were euthanized with an IC overdose of pentobarbital.

Injections: The injections were with sterile isotonic saline, performed with a syringe pump (AL-1000 from World Precision Instruments). The pump has a maximum pressure force of approximately 155 N. The injections were done with 50ml Syringes (Braun) through a 23G Butterfly (Kruuse) inserted manually in the sub cutis.

Tissue backpressure: A pressure sensor (iLoad mini-Dome 50lB from Loadstar Sensors) was mounted on the infusion pump to continuously measure and log the force applied by the pump to the syringe, during the infusion.

3D imaging: The induration was photographed with a Vectra H2 camera (Canfield). A baseline picture was obtained immediately before needle insertion. Following infusion, the bleb was photographed at 0m, 30m and 60m after injection.

DISCUSSION

Backpressure at these flow rates are prone to variation, as many factors play crucial roles (choice of syringe, needle gauge, insertion in the SC, viscosity). There were many incomplete injections, especially as the flow rate was increased, as it was superseding the capabilities of the syringe pump.

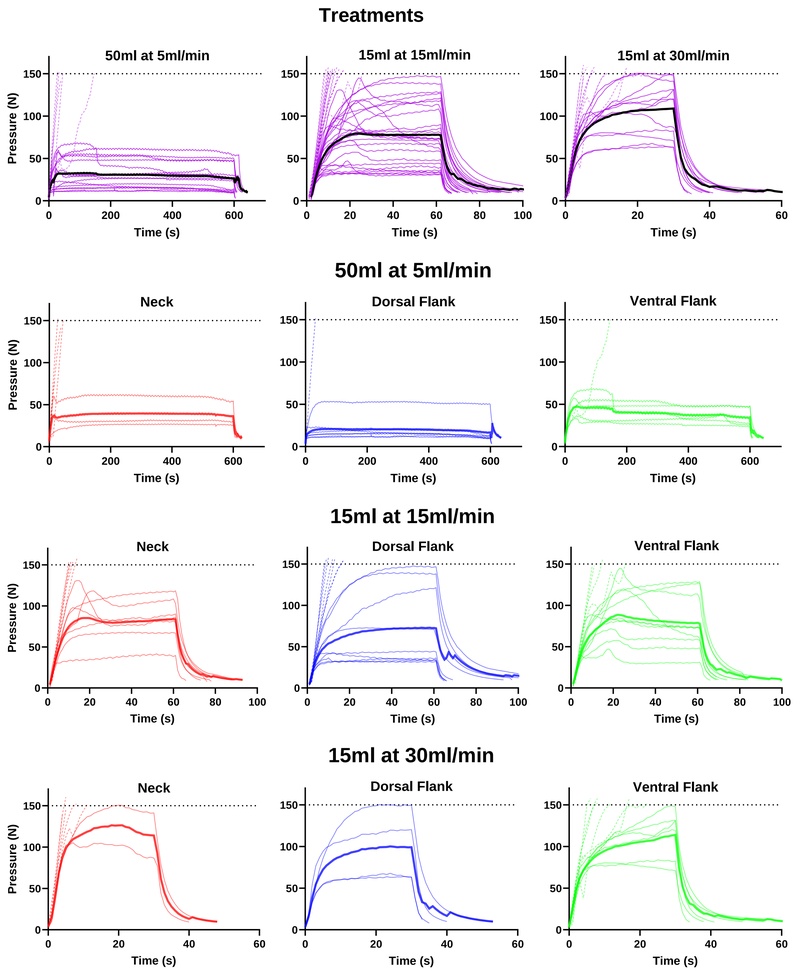
Quantification of the induration is feasible with 3D image analysis, however it's hampered by the fact that the animal must be anesthetized for the image acquisition, making it difficult to follow it for more than a few hours. The alignment of the animal (and later the 3D surfaces) over time, takes care and expertise and is prone to bias.

RESULTS

Back pressure

The pressure curves are separated into treatments (purple) and further separated into injection sites (RGB). Incomplete injections are shown as dotes lines.

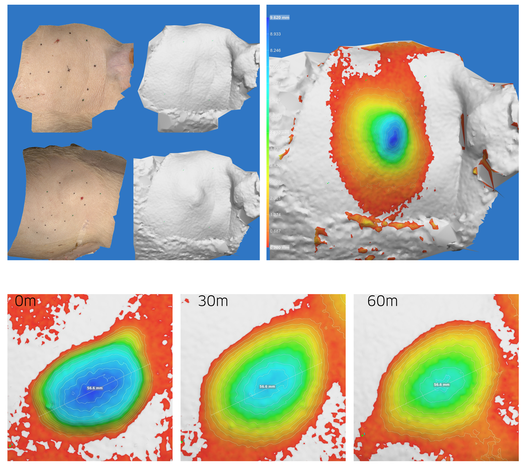
The syringe pump stalled at varying pressure rates at around 150N and above, giving rise to incomplete injections. 55 of the 92 injections were completed.



3D imaging

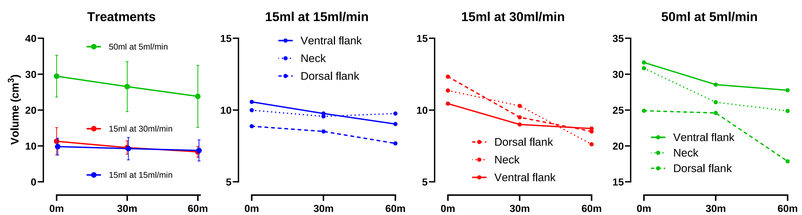
The height and volume of the induration is determined by manually aligning two surfaces and the software can calculate the maximum difference between the surfaces and the volume of the induration can be determined by drawing the boundary of the induration.

The topological differences between baseline and the timepoint are color-graded.



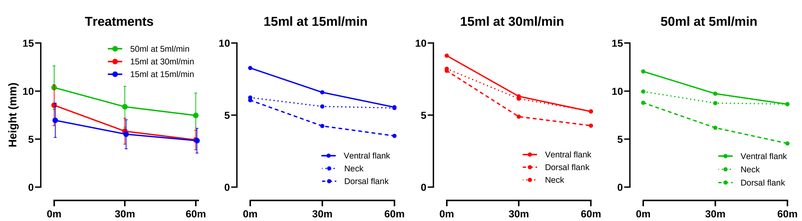
3D Induration volume

The volume of the induration from the different treatments are shown on the left. To the right the volume is separated into treatments and injection location.



3D Induration height

The height of the induration is plotted in the same manner as the volume.



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