# Craniospinal compliance of the juvenile pig is dependent on infusion method and location

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## Summary

Pigs are a favored pre-clinical model to study cerebrospinal fluid pressure (CSFP) dynamics in the context of spinal cord injury. Craniospinal compliance (CC) is a property that affects CSFP, but no reference values exist for pigs. We characterized the pig CC (pressure-volume index, PVI) using two different methods and measurement sites. In seven pigs, mean PVI ranged from 3.8 to 6.4 mL and was method- and site-dependent. The CC of the domestic pig (~23 kg) is considerably smaller than humans, and this should be considered in future translation of findings from pig models.

## Introduction

Spinal cord injury (SCI) is a devastating injury initiated by cord impingement, followed by cord swelling and stenosis of the intrathecal space (cerebrospinal fluid-filled space around the brain and spinal cord) [1]. Strategies for clinical management of SCI are important for improving patient outcomes. Animal models are critical for pre-clinical development of new SCI management strategies. Recent emerging interest in using cerebrospinal fluid pressure (CSFP) dynamics to monitor cord swelling and intrathecal stenosis has been investigated in pigs because of their size and anatomical similarities to humans [1,2]. However, the pig craniospinal compliance (CC, volume-buffering capacity, important property for CSFP dynamics) has not been characterized. Comparison of pig and human CC is required for clinical translation of pre-clinical findings. Additionally, CC is assessed by measuring the CSFP response to intrathecal volume infusions, but there is no consensus on the effect of different infusion methods and locations on CC. This study aimed to: 1) Determine reference CC for pigs; and, 2) Assess the effect of infusion method and location, on CC.

## Methods

Seven anaesthetized juvenile domestic pigs (23±2 kg) underwent surgery to place intrathecal catheters and pressure transducers for volume infusions and CSFP measurements, respectively (Fig. 1A, Ethics: SAM-24-011). Saline was infused using two methods [3]: bolus infusion of 2 mL at 0.25 mL/s (INF-B), and constant rate infusion at 0.025 mL/s until CSFP reached 60% of mean arterial blood pressure (INF-CR). Each infusion method was repeated three times at two sites: right lateral ventricle of the brain (V), and caudal spine intrathecal space at level of L3 (SCa). CSFP measurements were obtained at the infusion sites. CC was assessed using pressure-volume index (PVI, volume to induce a 10-fold increase in mean CSFP from baseline) [4]. Paired t-tests were used to compare PVI between infusion methods and locations.

## Results and Discussion

Using INF-B, PVI ranged from 3.8±0.4 to 5.0±1.8 mL. Using INF-CR, PVI ranged from 5.2±2.4 to 6.4±2.8 mL. Infusion location had an effect on PVI in INF-B (p=0.01) but not INF-CR (p=0.159, Fig.1B). Infusion method had an effect on PVI in the ventricle (p=0.011) but not the spine (p=0.111, Fig. 1C). Reference PVI in pigs is considerably smaller than in adult humans (PVI: 26.0±3.5 mL) [4]. CC assessed using PVI is both infusion method- and site- dependent.

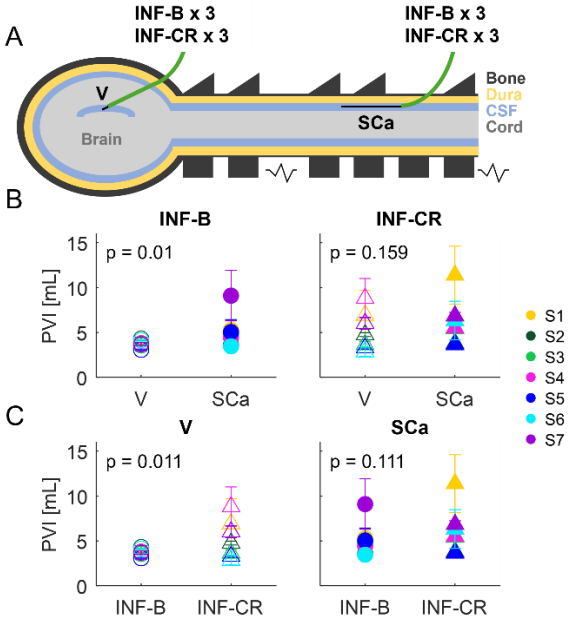


**Figure 1:** (A) Schematic of brain and spinal cord with infusion and CSFP measurement sites. Mean±SD PVI to compare infusion locations for each infusion method (B) and compare infusion methods for each infusion location (C) for subjects S1-S7.

## Conclusions

CC in the juvenile pig is considerably smaller than in humans; this should be considered when using this model for translational research related to CSFP dynamics. In assessing CC, or comparing CC measures between studies, differences in infusion method and infusion site should be reported and accounted for.

## References

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