

**Report on the project entitled: The Effect Of Chiari I Malformations
On CSF Flow In Cavalier King Charles Spaniels**

Funded by the American Cavalier King Charles Spaniel Club Charitable Trust

Stated objectives

1. Compare CSF flow velocity and distribution at the level of the foramen magnum between three groups of CKCS: normal CKCS, symptomatic CKCS with Chiari malformations and asymptomatic CKCS with Chiari malformations.
2. Estimate the incidence of asymptomatic Chiari I malformations in a small group of American CKCS.
3. Collect pedigree information and DNA from all study participants in collaboration with Dr. Rusbridge's study on the genetics of this disorder.

Original Budget: \$10,000. This was increased to \$20,000 in view of the excellent response to recruitment.

Summary of findings

There was an excellent response to the request for participants and ultimately we imaged 59 dogs (rather than the 30-45 we had originally hoped for). Imaging studies took 30 minutes to perform as long as everything went smoothly. The staff of the IAMS Pet Imaging Center worked extremely hard to help us meet the target number of patients to be imaged. We generated much more data than we expected, as the range of skull morphologies (skull shape) present required full characterization. The results of the study are therefore divided into firstly the morphological findings and their correlation to the presence of clinical signs and/or syringohydromyelia (SHM) and secondly the findings of the CSF flow measurements.

A) Morphological findings.

A set of definitions for the terms used has been added to the end of this report for clarification. One of the major problems we encountered was defining the limits of what

is normal versus abnormal. This has really not been done in a rigorous way previously and so we hope that we have helped to increase the knowledge in this area. Some of the parameters we evaluated we could measure and therefore document in an objective manner (e.g. the distance of cerebellar herniation) while others were more subjective.

- Of the 59 dogs that were imaged, 13 had neurological signs consistent with a Chiari Malformation (22%) and 46 were neurologically normal (78%).
- 51 of the 59 (86%) dogs had skull and cervical spinal morphologies that were classified as abnormal.
- These included:
 - a) Cerebellar indentation and crowding (55 dogs: 93% of cases).
 - b) Cerebellar herniation through the foramen magnum (50 dogs: 85% of cases). This varied from mild (1mm) to severe (> 4mm).
 - c) Occipital dysplasia causing enlargement of the foramen magnum (50 dogs: 85% of cases).
 - d) Syringohydromyelia (SHM) (22 dogs: 43% of cases). It is important to note that 13 dogs with SHM did show any clinical signs, they were neurologically normal.
 - e) Medullary kinking (33 dogs: 66% of cases).
 - f) A dorsal compressive lesion at the junction of the first and second cervical vertebrae causing significant spinal cord compression (12 dogs: 20% of cases). This was an unexpected finding and was felt to play a role in the genesis of SHM in some dogs with apparently mild indentation of the cerebellum.
- The volume of the caudal fossa and of the total cranial cavity were measured and the volume of the caudal fossa expressed as a percentage of the total cranial cavity. The volume of the caudal fossa is dictated by the occipital bone.
 - Both the absolute volume of the caudal fossa and the ratio of the caudal fossa to the whole cranial cavity were significantly smaller in dogs showing clinical signs. *This confirms that occipital hypoplasia plays an important role in this disease syndrome in CKCS.*
- Statistical evaluation of all of the morphological parameters was performed to determine the association of individual abnormalities, and the abnormalities when

considered together with the presence of SHM and with the presence of clinical signs.

- The following single parameters were significantly associated with the presence and severity of neurological signs:
 - Cerebellar indentation
 - Syringohydromyelia
 - Volume of the caudal fossa (absolute value and ratio).
- When considered together, the following parameters were highly predictive of neurological signs:
 - Cerebellar indentation, medullary kinking and ratio of caudal fossa volume/total cranial cavity volume.

Conclusions from the morphological study

1. The incidence of morphological abnormalities is high.
2. The incidence of SHM is also relatively high and is not always associated with clinical signs. In order to determine whether SHM always ultimately causes clinical signs, we will have to follow these dogs over time.
3. Occipital hypoplasia is present in dogs with clinical signs.
4. This type of brain malformation is multifactorial and includes abnormalities of the occipital bone (hypoplasia and dysplasia) causing cerebellar crowding and herniation, and abnormalities of the first and second cervical vertebrae and the articulation of C1 with the occipital bone. Medullary kinking appeared to result from both the occipital bone abnormalities and abnormalities of the cranio-cervical junction.

B) CSF Flow Measurement Findings:

We were able to evaluate CSF flow in all of our study dogs using Phase Velocity Contrast CINE MRI (PVC MRI), demonstrating the usefulness of this imaging modality for analyzing cerebrospinal fluid flow in veterinary patients. Peak velocities and CSF flow patterns were assessed in the ventral and dorsal subarachnoid spaces and within syrinxes at the following levels: just below the foramen magnum and within the cervical

spinal cord at the junction of the second and third cervical vertebrae (C2-C3 disc). Statistical evaluation of the observed flow characteristics was then performed.

Results were as follows:

- CSF flow could be better visualized and more effectively measured within the dorsal subarachnoid space if dogs were positioned for imaging with their head and neck flexed, mimicking a normal standing position, instead of the extended head and neck position used routinely for MRI imaging.
- Flow patterns could be visualized in both the sagittal (in-plane) and transverse (through-plane) views at all levels.
- Flow pattern observations included:
 - a) Obstruction to CSF flow was evident at the level of the foramen magnum in the majority of CKCS when compared with control dogs. This included clinically affected and unaffected Cavaliers, and varied from mild obstructions to a complete absence of observable flow at this level.
 - b) Obstruction to flow was also noted at the level of the C1-C2 dorsal compression if this lesion was present.
 - b) CSF flow was present within syrinxes, and peak flow velocities within syrinxes were often higher than within the corresponding subarachnoid space.
 - c) Turbulent flow and high-velocity jets were seen equally at the level of the foramen magnum, at the level of the cervical spinal cord, and within syrinxes. They were also seen most frequently in dogs with syringohydromyelia.
- Peak velocities of CSF flow were determined using transverse views. Velocity measurements demonstrated the following:
 - a) Peak velocities within the ventral and dorsal subarachnoid spaces were not significantly different between clinically affected and unaffected CKCS. However, affected dogs demonstrated a trend towards higher peak velocities within the dorsal subarachnoid space at the level of the foramen magnum.
 - b) Peak velocities were not significantly associated with the presence of syringohydromyelia at the level of the foramen magnum. However, peak velocities of CSF flow in the dorsal subarachnoid space were significantly lower at the level of the C2-C3 junction in dogs with syringohydromyelia.

- c) Additionally, when considered together, peak velocities within the dorsal subarachnoid space at the level of the foramen magnum and at the level of the cervical spinal cord were highly predictive of the presence of a syrinx, such that:
 - i) Higher peak velocities at the foramen magnum correlated with higher incidence of syringohydromyelia
 - ii) Lower peak velocities at the cervical spinal cord correlated with higher incidence of syringohydromyelia.
- d) We propose that this velocity gradient could be the result of obstruction to flow at the level of the foramen magnum and a relative post-obstructive expansion of the subarachnoid space and subsequent slowing of flow at the level of the cervical spine.
- e) Importantly, it was difficult to obtain measurements at the point of maximum obstruction at the foramen magnum, so measurements were obtained immediately caudal to this point in all CKCS. This limitation may have affected our ability to fully evaluate changes in peak velocities at the foramen magnum of CKCS.

Conclusions from the CSF flow study:

1. CSF flow patterns and velocities can be evaluated in dogs using PVC MRI.
2. Head position is important when performing these studies. A flexed head and neck imitating normal standing posture leads to a better determination of flow characteristics.
3. Obstruction to CSF flow at the foramen magnum is a component of Chiari malformations in CKCS.
4. In affected dogs, CSF flow velocity is high at the level of the FM and decreases over the C2-3 disc space, demonstrating a gradient of flow.
5. Quantitative assessment of CSF flow velocities may require more sophisticated software that is better able to measure flow within small regions of interest by taking measurements on a pixel – by – pixel basis, in order to allow evaluation at the point of maximal obstruction (at the foramen magnum).

Clinical relevance of CSF flow findings:

1. PVC MRI could be used pre-operatively to determine if obstruction(s) to CSF flow, turbulence, and/or high-velocity jets are present in CKCS with morphologic changes suggestive of a Chiari Malformation. This information could help neurologists and owners when deciding whether the observed clinical signs are due to the Chiari Malformation or if these morphologic findings are non-clinical. Such information could prove very useful in deciding the best course of treatment of such a patient.
2. Post-operatively, PVC MRI could be used to determine if obstruction(s) to CSF flow have been relieved by surgery or if additional surgery is warranted in patients with residual clinical signs.
3. The clinical progress of the study participants will be followed annually for 3 years and CSF flow velocities will be re-correlated with the development of clinical signs. This will be used to pursue a better understanding of velocity ranges that are predictive of clinically apparent disease.

Budget

The initial budget was \$10,000. This was increased to \$20,000 in view of the excellent response of breeders and owners to the request for cases. The total outlay of the project was \$16,777.55: \$15,000 on rental of MRI, anesthesia and MRI technician. \$1,777.55 was expended on supplies for DNA extraction and shipping of samples to Dr Rusbridge's collaborators. \$3,222.45 will be returned to the sponsoring agency.