BSAVA Congress 2018
5-8 April Birmingham, UK

Three-dimensional estimation of brain ventricular system volume in brachycephalic dogs with and without Chiari-like malformation and syringomyelia

C. Perrott [a], A. Coppi [a], E. Jovanovik [b], C. Rusbridge [ab]

[a] School of Veterinary Medicine, University of Surrey, Daphne Jackson Road, Guildford, Surrey, GU2 7AL, UK
[b] Fitzpatrick Referrals, Orthopaedics and Neurology, Halfway Lane, Eashing, Surrey, GU7 2QQ, UK

Introduction

Chiari-like malformation (CM) is a condition characterised by overcrowding of the caudal cranial fossa and craniocervical junction[1]. Overcrowding and herniation at the foramen magnum results in compression of subarachnoid space and disruption of cerebrospinal fluid (CSF) flow at the craniocervical junction. CM and associated CSF flow disruption is considered a major cause of ventricular dilation and syringomyelia (SM); fluid cavitation (syrinx) of the spinal cord[2].

Chiari-like malformation and syringomyelia (CM/SM) is common in brachycephalic toy breeds and the British Veterinary Association (BVA) and Kennel Club (KC) provide a CM/SM screening scheme which grades the presence of CM and SM on magnetic resonance imaging (MRI)[3]. Due to complex inheritance, current MRI screening cannot accurately predict whether offspring from two screened dogs will be affected by SM and the likely severity[4], making the condition difficult to eradicate. The BVA/KC CM/SM screening scheme was launched in 2012 but prior to this, unofficial screening was conducted which included assessment of ventricular dilation, which breeders feel is important. Absence of ventricular assessment in current BVA/KC screening due to lack of evidence of its ability to predict disease, is highly controversial amongst breeders. This poses the question; should the current BVA/KC CM/SM screening scheme be including ventricular assessment?

Objective

Compared to normal brachycephalic dogs, are brachycephalic dogs with Chiari-like malformation and syringomyelia more likely to have dilation of the lateral, third and fourth ventricles and expansion of the cavum velum interpositum (CVI) and quadrigeminal cistern?

Methods

Case control study that obtained quantitative volume measurements of ventricles using Cavalieri's principle of design-based stereology (Fig 1). Simpler linear measurements of the ventricles were also obtained, for comparison to more complex stereology based measurements (Fig 2).

Measurements were taken using T2-weighted sagittal brain MRI from 26 brachycephalic dogs. The sample was composed of a Chihuahua group; five with SM and five with normal MRI and a mixed brachycephalic toy breed group; eight with SM and eight breed matched with normal MRI.

Data analysis included descriptive statistics, Two-sample T-Test for parametric data and Mood's Median Test for non-parametric data. Pearson's product-moment correlation test assessed the association between volumetric stereology data and linear eFilm data.

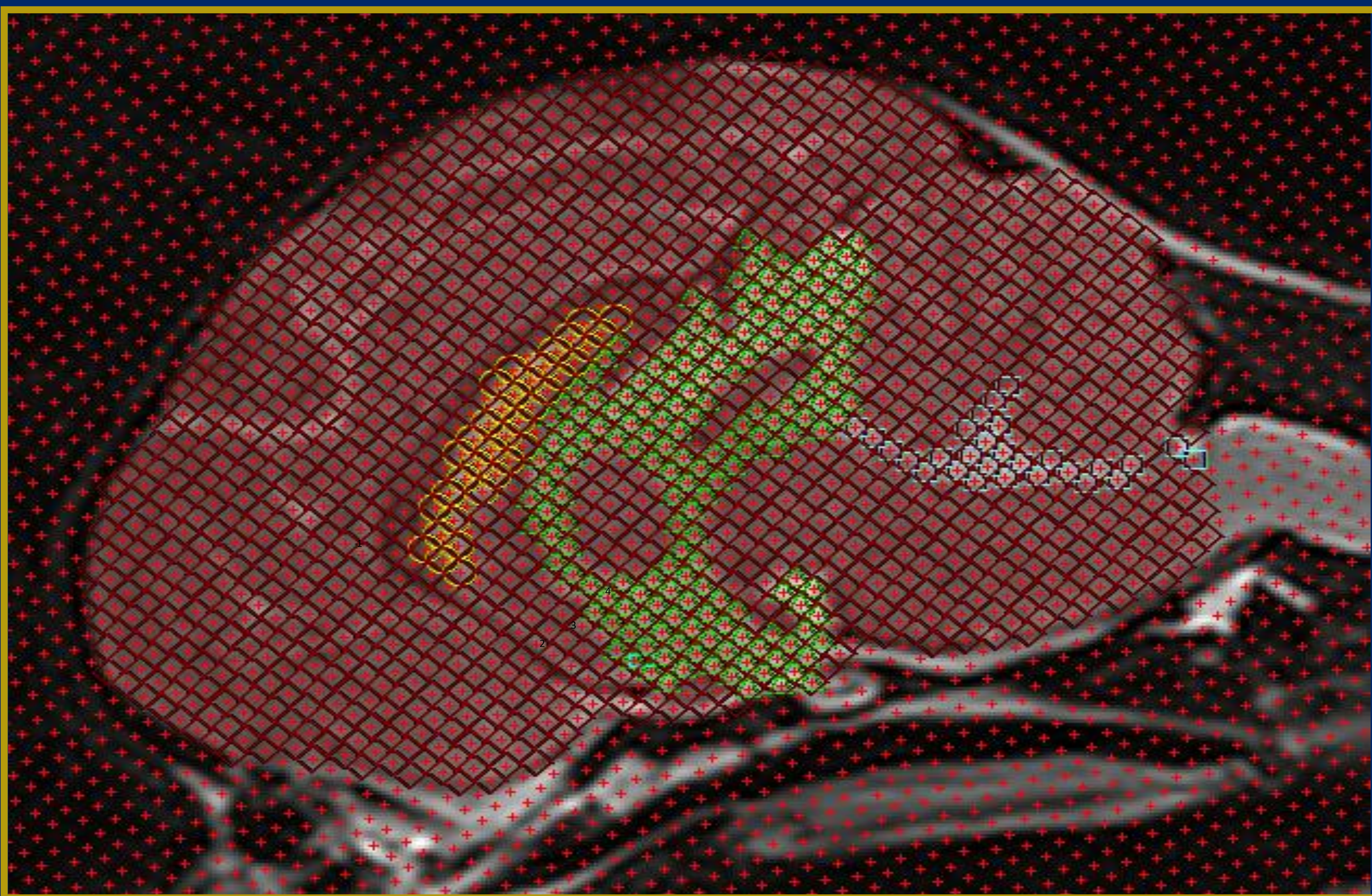

Figure 1: T2-weighted sagittal canine brain MRI with test-point grid overlaid by Stereo Investigator software. Volume measurement achieved by totalling grid points within structures of interest: total brain - brown, lateral ventricles – yellow, third ventricle (including CVI and quadrigeminal cistern) – green, fourth ventricle (including mesencephalic aqueduct) - blue. Point selection repeated on each MRI slice and then relevant quantities inputted into Cavalieri equation;
$\hat{V} = T \cdot \frac{a}{p} \cdot \sum_{i=1}^{M} Pi$ [5]

Figure 2: T2-weighted midsagittal canine brain MRI. eFilm linear measurements of: corpus callosum height (1), mesencephalic aqueduct height (2), fastigial recess width (3), fourth ventricle height (4).

Results

Stereology measurements showed no significant difference in lateral, third and fourth ventricle volume between Chihuahuas with and without CM/SM and mixed brachycephalic breeds with and without CM/SM.

eFilm measurements also showed no significant difference in the corpus callosum height, mesencephalic aqueduct height, fastigial recess width or fourth ventricle height between Chihuahuas with and without CM/SM and mixed brachycephalic breeds with and without CM/SM.

Comparison of stereology and linear measurements found a significant correlation between lateral ventricle volume and corpus callosum height for both Chihuahua and mixed brachycephalic breed groups. Significant correlations for the Chihuahua group also included lateral ventricles volume with mesencephalic aqueduct height and total brain volume with mesencephalic aqueduct height.
Significant correlations for the mixed brachycephalic breed group included fourth ventricle volume with fastigial recess width and total brain volume with corpus callosum height.

Impact

A novel design-based stereology methodology has successfully quantified ventricular volumes and may be applicable for future studies. Although stereology is considered superior and offers the benefits of unbiased volume estimation and low coefficient of error[6], the significant correlations between stereology and linear measurements could validate the linear method for some parameters. Linear measurements are likely to provide a simpler, more practical method to implement in practice for CM/SM screening.

Although ventriculomegaly is associated with CM/SM[4], currently a recommendation cannot be made that the BVA/KC CM/SM Health Scheme should include assessment of ventricular size.

Continued research is recommended, with an increase in sample size to reduce biological variability to further confirm whether assessment of ventricular size could provide added benefit and whether linear and stereological methods would be indeed equivalent. Additional screening methods for CM/SM are required to improve the health and welfare of predisposed breeds.

References:
1. Knowler, S. P. et al., 2014. Quantitative Analysis of Chiari-Like Malformation and Syringomyelia in the Griffon Bruxellois Dog. *PLOS ONE,* 9(2).
2. Rusbridge, C. & Knowler, S. P., 2004. Inheritance of occipital bone hypoplasia (Chiari type I malformation) in Cavalier King Charles Spaniels.. *Journal of Veterinary Internal Medicine,* 18(5), pp. 673-678.
3. BVA, 2014. *Chiari Malformation / Syringomyelia Scheme.* [Online] Available at: https://www.bva.co.uk/uploadedFiles/Content/Canine_Health_Schemes/Chiari_Malformation_Syringomyelia_Scheme.pdf [Accessed 5th October 2016].
4. Rusbridge, C., 2014. Chiari-like malformation and syringomyelia. *European Journal of Companion Animal Practice* , 23(3), pp. 70-89.
5. Howard, C. V. & Reed, M. G., 1998. *Unbiased Stereology, Three-dimensional Measurement in Microscopy.* 1st ed. Oxford : BIOS Scientific Publishers.
6. Baddeley, A. & Vedel Jensen, E. B., 2004. *Stereology for Statisticians.* 1st ed. Hoboken: Taylor and Francis.