RESEARCH PROGRESS REPORT SUMMARY

Grant 02131: Neurostimulation: A Groundbreaking New Treatment for Canine Epilepsy

Principal Investigator: Dr. Sam Nicholas Long, BVSc, PhD

Research Institution: The University of Melbourne

Grant Amount: $116,000.00

Start Date: 10/1/2014 **End Date:** 9/30/2017

Progress Report: End-Year 2

Report Due: 9/30/2016 **Report Received:** 11/15/2016

Recommended for Approval: Approved

(Content of this report is not confidential. A grant sponsor's CHF Health Liaison may request the confidential scientific report submitted by the investigator by contacting the CHF office. The below Report to Grant Sponsors from Investigator can be used in communications with your club members.)

Original Project Description:

Epilepsy is a debilitating condition that affects a large number of dogs, resulting in premature death and distress for their owners. For many dogs the underlying cause is unknown. In people, advances in some types of imaging have identified subtle abnormalities, including abnormal development and shrinkage of particular regions in the brain of some people with epilepsy that can be surgically removed to improve the control of seizures. This project will apply the same advanced techniques to the brains of dogs with epilepsy to determine whether those same abnormalities exist in dogs. In those dogs in whom no abnormalities can be found, this project will investigate a new form of treatment, known as neurostimulation which has been shown to reduce the frequency of seizures dramatically in human clinical trials. This involves surgically implanting a new, highly sophisticated device called the Brain Radio that can provide controlled electrical stimulation to parts of the brain while simultaneously recording the brain's activity. This device is one of the very first that could potentially provide successful therapy only when needed to treat imminent seizures and if it proves successful in dogs it will enter clinical trials in people with epilepsy.

Grant Objectives:

The objectives of the discovery phase are:

1) to develop a three-dimensional population based canine brain MRI atlas using volumetric techniques, MR spectroscopy and diffusion weighted imaging-based tractography

2) to use the population based canine brain MRI atlas for computer-assisted morphometry to detect subtle neuromorphologic change in dogs with idiopathic epilepsy

3) to use magnetic resonance spectroscopy for in-vivo investigation of changes in cerebral metabolites in dogs with idiopathic epilepsy

Publications:

Description of technique and lower reference limit for magnetic resonance imaging of hippocampal volumetry in dogs. Milne ME, Anderson GA, Chow KE, O'Brien TJ, Moffat BA, Long SN. Am J Vet Res. 2013 Feb;74(2):224-31. doi: 10.2460/ajvr.74.2.224.

Development of representative magnetic resonance imaging-based atlases of the canine brain and evaluation of three methods for atlas-based segmentation. Milne ME, Steward C, Firestone SM, Long SN, O'Brien TJ, Moffat BA. Am J Vet Res. 2016 Apr;77(4):395-403. doi: 10.2460/ajvr.77.4.395.

Report to Grant Sponsor from Investigator:

Pioneering computer processing techniques have been developed by the researchers to allow formation of a composite 'canine brain atlas' to help identify subtle abnormalities in the epileptic dog brain. These processing techniques have been tested with conventional MRI scans and are now being applied to the brains of dogs with epilepsy. Using these advanced techniques we will be able to take look at the brain in 3 ways:

1) High resolution images of the brain to define normal structures (the shape and size of grey and white matter)
2) Images of nerve pathways that exist in the brain (using a technique called tractography)
3) Evaluating signaling chemical profiles in the brain

To date, these sequences have been used to characterise the brain of normal dogs, along with dogs with epilepsy identified for the study. The first 6 epileptic dogs have been scanned so far with a total of 14 dogs scheduled to be completed by the end of 2016. Although case

recruitment has been continuing, we have encountered a slight delay in data acquisition due to our chief researcher, Dr Milne, taking maternity leave. Preliminary data has been examined and some work detail commencing the atlas. Importantly, we have demonstrated that a new way of performing tractography (Constrained Spherical Deconvolution or CSD) is possible to perform on the brain of dogs with epilepsy and that it provides very high resolution images of the white matter pathways of dogs – the normal dogs scanned so far have been used as part of a Masters thesis which has been published by one of our students, Renee Mineo.