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SHORT COMMUNICATION

# Feasibility study of a caregiver seizure alert system in canine epilepsy

**Lisa D. Coles**[a,*], **Edward E. Patterson**[b,2], **W. Douglas Sheffield**[c,3], **Jaideep Mavoori**[c,3], **Jason Higgins**[c,3], **Michael Bland**[c,3], **Kent Leyde**[c,3], **James C. Cloyd**[a,1], **Brian Litt**[d,4], **Charles Vite**[e,5], **Gregory A. Worrell**[f,6]

[a] *University of Minnesota, College of Pharmacy, Minneapolis, MN, USA*
[b] *University of Minnesota, Veterinary Medical Center, St. Paul, MN, USA*
[c] *NeuroVista, Seattle, WA, USA*
[d] *University of Pennsylvania, Bioengineering and Neurology, Philadelphia, PA, USA*
[e] *University of Pennsylvania, Veterinary Medical Center, Philadelphia, PA, USA*
[f] *Mayo Clinic, Rochester, MN, USA*

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**Summary** A device capable of detecting seizures and alerting caregivers would be a major advance for epilepsy management, and could be used to guide early intervention and prevent seizure-related injuries. The objective of this work was to evaluate a seizure advisory system (SAS) that alerts caregivers of seizures in canines with naturally occurring epilepsy. Four dogs with epilepsy were implanted with a SAS that wirelessly transmits continuous intracranial EEG (iEEG) to an external device embedded with a seizure detection algorithm and the capability to alert caregivers. In this study a veterinarian was alerted by automated text message if prolonged or repetitive seizures occurred, and a rescue therapy protocol was implemented. The

* Corresponding author at: Center for Orphan Drug Research/Experimental and Clinical Pharmacology, Room 4-226, McGuire Translational Research Facility, 2001 6th Street SE, College of Pharmacy, University of Minnesota, Minneapolis, MN 55455, USA. Tel.: +1 612 624 1861; fax: +1 612 626 9985.
*E-mail addresses:* durh0016@umn.edu (L.D. Coles), patte037@umn.edu (E.E. Patterson), wdsheffield@gmail.com (W.D. Sheffield), jmavoori@hotmail.com (J. Mavoori), jason.higgins11@gmail.com (J. Higgins), mike.r.bland@gmail.com (B. Michael), kent.leyde@gmail.com (K. Leyde), cloyd001@umn.edu (J.C. Cloyd), littb@mailmedupenn.edu (B. Litt), WorrellGregory@mayo.edu (G.A. Worrell).
[1] Center for Orphan Drug Research/Experimental and Clinical Pharmacology, 2001 6th Street SE, College of Pharmacy, University of Minnesota, Minneapolis, MN 55455, USA.
[2] Veterinary Clinical Sciences, 1365 Gortner Avenue, St Paul, MN 55108, USA.
[3] NeuroVista Corporation, 100 Fourth Avenue North, Suite 600, Seattle, WA 98109, USA.
[4] Department of Bioengineering, 301 Hayden Hall, 3320 Smith Walk, University of Pennsylvania, Philadelphia, PA 19104, USA.
[5] School of Veterinary Medicine, University of Pennsylvania, 3900 Delancey Street, Philadelphia, PA 19104-6010, USA.
[6] Department of Neurology, Mayo Systems Electrophysiology Laboratory, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA.

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performance of the SAS caregiver alert was evaluated over the course of 8 weeks. Following discontinuation of antiepileptic drugs, the dogs experienced spontaneous unprovoked partial seizures that secondarily generalized. Three prolonged or repetitive seizure episodes occurred in 2 of the dogs. On each occasion, the SAS caregiver alert successfully alerted an on call veterinarian who confirmed the seizure activity via remote video-monitoring. A rescue medication was then administered and the seizures were aborted. This study demonstrates the feasibility of a SAS to alert caregivers to the occurrence of prolonged or repetitive seizures and enables rescue medications to be delivered in a timely manner. The SAS may improve the management of human epilepsy by alerting caregivers of seizures, enabling early interventions, and potentially improving outcomes and quality of life of patients and caregivers.


## Introduction

Poorly-controlled epilepsy represents a significant risk for injury and death as well as large economic burden (Manjunath et al., 2012; Sperling, 2004). Sudden unexplained death in epilepsy (SUDEP) may be a consequence of unwitnessed repetitive or prolonged seizures in vulnerable patients (Ficker, 2000; Sperling et al., 1999; Tomson et al., 2005). The ability to accurately monitor and quantify the occurrence, duration, and intensity of seizures should improve the management of patients, help prevent seizure-related injuries, and may provide a strategy to prevent SUDEP. In addition, a device capable of accurately detecting seizures should prove useful for evaluation of AED and other therapies, since patient reporting of seizures and their diaries are known to be inaccurate (Hoppe et al., 2007). Moreover, non-convulsive seizures are often unrecognized by patients but may contribute to complications arriving from epilepsy (Dunne et al., 1987).

A seizure advisory system (SAS) capable of alerting patients and caregivers about seizures has been developed. The SAS is an implantable device that wirelessly transmits intracranial EEG (iEEG) from 16 implanted electrodes to an externally worn processing unit for storing continuous iEEG, analysis, and communicating results to patient or caregiver via text messaging (Fig. 1). A previous study evaluated the performance of the seizure detection algorithm embedded in the SAS device in dogs with naturally occurring partial epilepsy (Davis et al., 2011). In this study, we use the SAS to deliver automated caregiver alerts via text-messaging to an on call veterinarian for acute repetitive or prolonged seizures.

While there are many animal models of epilepsy (Pitkanen and McIntosh, 2006; Sarkisian, 2001) the majority require the use of a chemical or physical insults resulting in seizures which may significantly differ from human epilepsy (Sarkisian, 2001). In contrast, naturally occurring canine partial epilepsy is an excellent model for human epilepsy because of the clinical (Berendt et al., 1999; Chandler, 2006; Jeserevics et al., 2007; Pellegrino and Sica, 2004) and pharmacological (Leppik et al., 2009; Volk et al., 2008) similarity to human focal epilepsy. Importantly, dogs are large enough to accommodate the implantable SAS device, designed for humans, tested in this study (8).

The same principles of AED therapy apply to dogs and humans, although the altered metabolism and rapid elimination of some AEDs dictates the use of a subset of drugs in dogs. Approximately 25% of epileptic dogs remain uncontrolled, which is a rate comparable to humans (11—15). Based on these observations, dogs with naturally occurring epilepsy are good candidates for evaluating a seizure advisory system. The purpose of this study was to evaluate the SAS for alerting a veterinarian to acute repetitive or prolonged seizures in dogs with epilepsy. This work is a critical step toward evaluating the ability of a seizure monitoring system to alert patients/caregivers and initiate an intervention. In the future, a similar system implementing seizure forecasting algorithms may allow medications to be given to prevent seizure occurrence.

## Methods

Five dogs with naturally occurring idiopathic epilepsy were implanted with SAS devices as previously described, Fig. 1 (8). This study was approved by the University of Minnesota Institutional Animal Care and Use Committee. The dogs were housed in a canine epilepsy monitoring unit (EMU) with continuous recorded video. Phenobarbital therapy was withheld which resulted in naturally occurring seizures. Over an 8-week period, seizure activity was documented by review of the SAS device output, and validated by expert visual review of iEEG data and video recordings.

The SAS was programmed to alert an on-call veterinarian (NP) via an automated text-message when prolonged (single seizure lasting longer than 5 min) or repetitive seizures (2 or more seizures within 1 h,or 3 or more seizures within 4 h) were detected. The on-call veterinarian (NP) confirmed the seizure activity via remote video-monitoring when alerted to prolonged or repetitive seizures. In the event of prolonged or repetitive seizures, a rescue therapy protocol was initiated consisting of diazepam (0.5 mg/kg) or phenobarbital (6 mg/kg) administered as single IV dose via an indwelling catheter or vascular access port. Blood samples (2—5 mL) were collected at 30,60, and 120 min following dosing. All blood samples were placed on ice immediately and centrifuged to separate plasma. Plasma samples were frozen at −20 °C for later analysis of plasma drug concentration.

### Analysis of AEDs in plasma

Drug concentrations of the rescue therapy (phenobarbital and diazepam) were measured in the plasma samples using validated HPLC-UV methods. Phenobarbital and diazepam were extracted from 0.25 mL of plasma via liquid—liquid extraction. Phenytoin and nordiazepam were used as internal standards for phenobarbital and diazepam, respectively.