

**TITLE:** Neurophysiology and Forecasting Seizures

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The unpredictability of seizures and the adverse cognitive and physical side effects associated with AEDs, are the most disabling aspects of epilepsy. We now have evidence from humans that seizures are not random events, but rather are associated with intracranial EEG (iEEG) changes that occur tens of minutes to hours before clinical events. This research has led NeuroVista Inc. to develop a seizure advisory system (SAS) that uses iEEG and machine learning algorithms to track the probability of seizure occurrence. Using patient specific algorithms NeuroVista's SAS can forecast periods of increased and decreased seizure likelihood with high sensitivity and specificity, benchmarked against a chance predictor. NeuroVista's SAS has been validated in humans undergoing iEEG monitoring for epilepsy surgery, and has recently been approved for a human pilot clinical trial in Australia.

We have recently proposed to use the NeuroVista's SAS device to guide the delivery of AEDs. We hypothesize that intelligent delivery of AEDs at times of increased seizure likelihood will effectively prevent clinical seizures. During periods of low seizure likelihood AEDs would not be required, reducing side effects. In this proposal we develop and test neurophysiologically-based responsive pharmacotherapy in naturally occurring canine epilepsy as the first step in creating a new treatment paradigm for medically resistant human partial epilepsy. Naturally occurring canine partial epilepsy is an ideal model for developing this therapy because of the clinical, physiological, and pharmacological similarities between canine and human partial epilepsy. In addition, dogs are large enough to tolerate implantation of the human SAS device.