An interview with Sharon Chiang, 2019 Epilepsia Open Prize Winner for Clinical Research

1 | WHO ARE YOU? (PROVIDE SOME BACKGROUND—YOUR EDUCATION, TRAINING, PRESENT POSITION, ANY RELEVANT PERSONAL INTERESTS)

I am a statistician and neurology physician resident in the Department of Neurology at the University of California, San Francisco. I received my M.D. from Baylor College of Medicine in Houston, Texas, and received my Ph.D. in Statistics from Rice University in Houston, Texas. During my Ph.D., I worked on developing new Bayesian statistical methods for estimating connectivity networks and integrating multimodal spatiotemporal datasets into improving statistical variable selection procedures, including resting-state functional magnetic resonance imaging (fMRI), structural MRI, and positron emission tomography (PET) imaging. I am interested in the development of new statistical methods and application of existing methods for seizure risk estimation, focus localization, network modeling, and neuromodulation.

2 | WHAT GOT YOU INTERESTED IN EPILEPSY RESEARCH?

I have wanted to be a neurologist since my first year of medical school. My interest in becoming an epileptologist and go into epilepsy research first started after I saw a patient have a seizure, which struck a chord for me as to the impact that epilepsy has on people, and has guided my research interests ever since. I chose to pursue my Ph.D. in statistics to acquire the skills to develop cutting edge models for epileptic networks to understand when and why seizures occur. During my Ph.D., I received strong influence from my clinical mentors, Dr. Zulfi Haneef and Dr. John Stern. Their mentorship was paramount throughout my Ph.D. and informing my research direction, as they exemplify physicians who use their compassion and clinical acumen in what they see in clinic to guide their research questions. During my Ph.D., I worked with my statistics Ph.D. advisor, Dr. Marina Vannucci, to develop several new Bayesian statistical models for integrating fMRI with presurgical PET imaging to predict which patients with temporal lobe epilepsy (TLE) would benefit from anterior temporal lobe resections, as well as a new Bayesian model for estimating effective connectivity networks in TLE. Since that time, my clinical interest and research questions in epilepsy have continued to grow together. Since getting to know more people with epilepsy and their families, I am learning more and more about the depth of the impact that epilepsy has on people. My current interests in epilepsy research are focused on developing statistical models that can help provide solutions to issues that greatly affect people with epilepsy, including the unpredictability of seizures, focus localization, and neuromodulation.

3 | EXPLAIN FOR OUR GENERAL READERSHIP WHAT QUESTION YOUR STUDY ADDRESSED AND HOW DID YOU GO ABOUT DESIGNING YOU STUDY?

Seizure unpredictability plays a large role in the burden of epilepsy for people with epilepsy and their caregivers. Currently, clinical monitoring and treatment decisions are based on the observed number of seizures and changes that patients report in seizure frequency from visit to visit. However, one of the fundamental challenges in treating epilepsy is that observed seizure frequencies may not necessarily reflect changes in seizure risk, but rather expected probabilistic variation.
around an unchanged seizure risk state. There is currently no systematic way to identify when changes in seizure count reflect an actual change in the person's underlying seizure risk. Therefore, we developed a new statistical method, the Epilepsy Seizure Assessment Tool (EpiSAT), based on latent state modeling. This new method permits estimation of underlying seizure risk from patient-reported seizure frequencies on the individual patient level, while simultaneously accounting for triggers and other covariates in their impact on seizure threshold.

To develop this model, we worked with SeizureTracker.com, which is an online and mobile seizure diary that serves over 20,000 people with epilepsy, and is currently one of the world's largest patient-reported seizure diary databases. We statistically validated our model on simulated seizure diary and then tested it on 44,697 seizures recorded in SeizureTracker.com from 105 patients with tuberous sclerosis complex.

4 | WHAT WERE THE RESULTS AND HOW DO YOU INTERPRET YOUR FINDINGS?

We found that EpiSAT is able to accurately determine which changes in seizure frequency are caused by true changes in the patient's underlying seizure risk level, and can distinguish these from changes caused by natural variation. Compared to approaches where providers do not explicitly model underlying states, we found that EpiSAT consistently yields more accurate identification of seizure risk, which in clinical practice would be anticipated to help decrease the number of unnecessary medication adjustments. In patients with tuberous sclerosis complex (TSC), we found evidence of four underlying seizure risk states. The expected duration of each seizure risk state was less than 12 months for each state, which supports the guideline of using 12 months for seizure freedom. Overall, our study shows that a new view of seizure burden which is based on statistical estimation of seizure risk may help avoid conflation of changes caused by natural history from changing seizure burden. Our hope is that, if incorporated into clinical practice, it may help decrease unnecessary medication dose changes when attempting to achieve seizure control.

5 | WHAT NEXT STEPS IN EPILEPSY RESEARCH ARE YOU TAKING AND WHAT ARE YOUR CAREER GOALS?

We are currently investigating further properties of EpiSAT and performing more extensive validation studies to test clinical utility. The upcoming results of these investigations will reveal how EpiSAT performs in actual clinical practice for assessing seizure risk. The potential clinical utility of EpiSAT is as a new clinical decision support tool that can be used by clinicians to guide medication treatment decisions and to help reduce the unpredictability of seizures by providing an approach that can estimate seizure risk.

The next steps in my career path are to complete my neurology residency training. After this, I plan to pursue postdoctoral training in statistics in addition to epilepsy fellowship. In the long term, I would like to become an independent investigator and physician-scientist, focusing on developing statistical methods that can address issues that people with epilepsy face.

6 | WHAT DOES THE EPILEPSIA OPEN PRIZE MEAN FOR YOU, YOUR LABORATORY, RESEARCH INSTITUTE, AND YOUR FUTURE?

I am extremely honored that our research team has received the prestigious 2019 Epilepsia Open Prize. This prize is an honor for our Statistics laboratory at Rice University, and on behalf of all of the members of our research team, we express our deepest gratitude. We hope that the awarding of this prize and our research will help bring more attention to the need of people with epilepsy for rigorous statistical models and statistical software that can help reduce the unpredictability of seizures. As an aspiring epileptologist and young researcher, my future research career will be greatly enhanced by the Epilepsia Open Prize. I would like to express my gratitude to our research team: Dr. Marina Vannucci, Dr. John Stern, Dr. Daniel Goldenholz, and Co-founder of SeizureTracker.com Robert Moss, for making this research possible.

Read the winning article “Epilepsy as a dynamic disease: A Bayesian model for differentiating seizure risk from natural variability.”

Aristea S. Galanopoulou Editor-in-Chief
Dong Zhou Editor-in-Chief
Epilepsia Open
Email: aristea.galanopoulou@einstein.yu.edu

ORCID

Dong Zhou https://orcid.org/0000-0001-7101-4125

REFERENCES

1. Chiang Sharon, Guindani Michele, Yeh Hsiang J, Dewar Sandra, Haneef Zulfi, Stern John M, Vannucci Marina. A hierarchical bayesian model for the identification of PET markers associated to the prediction of surgical outcome after anterior temporal lobe resection. Front Neurosci. 2017;11:669.
2. Chiang Sharon, Guindani Michele, Yeh Hsiang J, Haneef Zulfi, Stern John M, Vannucci Marina. Bayesian vector autoregressive model for multi-subject effective connectivity inference using multi-modal neuroimaging data. Hum Brain Mapp. 2017;38:1311–1332.

3. Chiang Sharon, Vannucci Marina, Goldenholz Daniel M, Moss Robert, Stern John M. Epilepsy as a dynamic disease: a Bayesian model for differentiating seizure risk from natural variability. Epilepsia Open. 2018;3:236–246.