Results: A total of 205 CIED interrogations were performed in 139 patients (age 69±14 years; 54% female). The primary objective was met in 42% of CIED interrogations, including detection of atrial or ventricular arrhythmias (34%), lead dislodgement/failure to capture (3%), pacemaker mediated tachycardia (0.5%) and elective replacement interval (3.9%). OAC was initiated in 8% of patients and changes in medical treatment or need for additional testing (not related to the CIED) was performed in 52% of the CIED interrogations.

Conclusion: The use of remote assistance device can have a significant social and clinical impact on rural populations by providing highly specialized health care to patients in difficult to reach areas. Moreover, the use of remote assistance overcomes the current difficulties associated with remote monitoring (i.e. inability to change device programming).

Results: In the total of 15 patients, a minimum esophageal temperature below 25 °C was recorded in 8 cases during cryoablation. The lowest esophageal temperature did not occur in the same sensor for all cases or even freezes in the same patient. Sensor 7 recorded the coldest temperature in 7/15 of these freezes, Sensor 8 recorded 3/15, Sensor 10 recorded 2/15, and Sensors 4, 5, and 10 recorded one each. When compared to neighboring sensors, the largest difference between neighboring sensors was 13.14 degrees, with a range of 5.6 to 19.9 degrees.

Conclusion: The disparity between neighboring temperature sensors suggest that single sensor probes are insufficient to detect the lowest temperature of the esophagus. Continuation of cryoablation to very low temperatures could increase risk of collateral injury to the esophagus. Use of multi-sensor temperature probes helps in accurately reflecting the coldest temperature point of the esophagus during cryoablation. Similar discrepancy may also be seen in radiofrequency ablation.

PO-615-08

SINGLE SENSOR VERSUS MULTI-SENSOR ESOPHAGEAL MONITORING: WHAT ARE WE MISSING?

Kristin Babb PAC; Emrie D. Tomaiko BA; Jake Martinez DO; Rong Bai MD, FHRS; Michael S. Zawaneh MD; Roderick Tung MD, FHRS; J. Peter Weiss MD, MSci, FHRS and Wilber W. Su MD, FHRS

Background: Esophageal temperature monitors are often used to decrease risk of esophageal injury during atrial fibrillation ablation. Multi-sensor monitors have been shown to have a superior thermodynamic profile in radiofrequency ablation, but there is limited data on single versus multi-electrode temperature discrepancies in cryoballoon ablation.

Objective: We aim to evaluate temperature differences in the Circa S-Cath, a multi-sensor esophageal probe, to investigate its potential benefits over a single sensor probe in cryoablation.

Methods: A total of 15 patients underwent cryoballoon ablation for atrial fibrillation under general anesthesia. A Circa probe was placed oropharyngeally after intubation. The Circa Esophageal Temperature Monitor has 12 sensors total located 8mm apart. Each sensor has a radiopaque marker and collects a temperature to the nearest 10th of a degree every half second. Position of the Circa probe could be adjusted under fluoroscopy.

Results: The total of 15 patients, a minimum esophageal temperature below 25 °C was recorded in 8 cases during cryoablation. The lowest esophageal temperature did not occur in the same sensor for all cases or even freezes in the same patient. Sensor 7 recorded the coldest temperature in 7/15 of these freezes, Sensor 8 recorded 3/15, Sensor 10 recorded 2/15, and Sensors 4, 5, and 10 recorded one each. When compared to neighboring sensors, the largest difference between neighboring sensors was 13.14 degrees, with a range of 5.6 to 19.9 degrees.

Conclusion: The disparity between neighboring temperature sensors suggest that single sensor probes are insufficient to detect the lowest temperature of the esophagus. Continuation of cryoablation to very low temperatures could increase risk of collateral injury to the esophagus. Use of multi-sensor temperature probes helps in accurately reflecting the coldest temperature point of the esophagus during cryoablation. Similar discrepancy may also be seen in radiofrequency ablation.

PO-616-01

ROTOR LOCALIZATION AND PHASE MAPPING OF CARDIAC EXCITATION WAVES USING DEEP NEURAL NETWORKS

Jan Lebert MSc; Namita Ravi; Flavio H. Fenton PhD and Jan Christoph PhD

Background: Finding sources of arrhythmias is challenging due to low resolution and noise associated with various cardiac mapping approaches. Deep learning algorithms provide a novel paradigm to overcome these challenges.

Objective: We hypothesized that a convolutional neural network (CNN) can be trained to predict phase maps and phase singularities (PS) from short spatio-temporal sequences of electrical excitation wave patterns.

Methods: Rabbit and pig optical mapping recordings of ventricular fibrillation (VF) as well as very noisy, low-resolution, and extremely sparse simulated data of reentrant wave chaos mimicking multi-electrode catheter or optical fiber recordings were used to train and evaluate a CNN with an encode-decoder architecture. The CNN predicts either phase maps or PS positions from ≤ 10 snapshots of excitation wave patterns.

Results: The CNN was able to robustly predict phase maps for both optical mapping data as well as simulated data with accuracies of about 95% and can be performed even in the presence of strong noise and highly sparse or incomplete data. Predictions can also be performed across different data, with a CNN being trained on one species and then successfully applied to another, or being trained on simulated data and then applied to experimental data. It appears that the deep learning algorithm learns to associate phase patterns with a broad class of excitable spatio-temporal activity, and understands the more generalized phase mapping problem, independent of physiological parameters or species-dependent wave dynamics. We were able to predict PS positions either directly by the CNN or indirectly, by computation from the predicted phase maps. We found that the indirect prediction of PS positions was more robust in experimental data.

Conclusion: CNNs present a powerful method to analyze the dynamics of complex reentrant wave patterns and to overcome the challenges associated with low spatial resolution and very noisy recordings. Future uses may include the mapping of atrial fibrillation in the clinical setting.
Background: cAMP is key for transducing autonomic signals and compartmentalization of cAMP signaling. Yet, if cAMP signaling occurs heterogeneously throughout the intact heart, and how this translates into functional responses, has not been explored.

Objective: To determine the spatiotemporal kinetics of cAMP activity in basal regions vs. the apex (n=5) in male and female cardiac-specific CAMPER reporter hearts.

Results: In male hearts, cAMP was uniformly activated in response to β-AR stimulation with bolus norepinephrine (NE, 1.5 μM). Conversely, in female hearts NE led to a greater change in cAMP activity in the apex vs. base in both female (n=7, p<0.05) and male hearts (n=5, p<0.05). Likewise, PDE activity assays showed higher total PDE activity in apical regions (n=10, p<0.01) with more apical PDE activity in female vs. male hearts (n=5, p<0.05). In female hearts, faster apical cAMP deactivation following bolus NE was associated with a significant difference in action potential duration (APD90) between apex and base (n=3, p<0.05), but APD90 was not significantly different between regions in male hearts.

Conclusion: Using novel whole heart imaging, we have shown female hearts display lower maximal cAMP activity and faster deactivation in the apex, in part, due to elevated PDE activity in this region. This heterogeneity was not observed in male hearts. These findings may have important implications for electrophysiological responses regulated by the cAMP pathway, particularly in heart failure, where PDE activity is altered.

PO-616-03
HIGH-THROUGHPUT SCREENING TO IDENTIFY DRUGS THAT CAN TREAT LONG QT SYNDROME CAUSED BY TRAFFICKING-DEFICIENT K,11.1 (HERG) VARIANTS
Christian Egly PharmD; Brian P. Delisle PhD; David C. Weaver PhD and Bjorn C. Knollmann MD, PhD

Background: The potassium channel K,11.1 plays an important role in repolarization of cardiac action potentials and loss-of-function (LOF) K,11.1 variants cause Long QT Syndrome which predisposes individuals to fatal cardiac arrhythmias. About 90% of LOF mutations prevent K,11.1 intracellular transport (trafficking) to the plasma membrane and prolonged incubation with drugs can sometimes increase K,11.1 trafficking and restore K,11.1 current (I,K,11.1).

Objective: Develop an optimized thallium (Tl⁺)-flux assay to screen a library of clinically approved drugs for increased trafficking of two K,11.1 potassium channel variants.

Methods: We developed a novel Tl⁺-based fluorescent assay and HEK-293 cells expressing K,11.1 trafficking-deficient variants (K,11.1-G601S-G965*X and K,11.1-N470D) to screen 1900 drugs (three replicates each) for increased K,11.1 trafficking. HEK-293 cells were plated on 384-well clear bottomed plates with 10 μM drug in individual wells 24-hours before experiments. On the day of experiments, drug was washed out, loaded with thallium-sensitive dye, and imaged using a 384-well fluorescent plate reader. Drug hits were detected using the slope of fluorescence in the assay and calculating the median and median absolute deviation (MAD).

Results: The screen detected a total of 80 drugs (average >3 MADs) that increased K,11.1 trafficking in both variants. Most drugs that increase K,11.1 trafficking inhibit the channel acutely, so we next screened acute and 24-hour drug effects on K,11.1-WT channel and eliminated drugs that block the channel. Concentration response curves (1 nM to 25 μM) were generated from 40 drugs that had <20% acute block at 10 μM, a tolerable side effect profile and increased trafficking of K,11.1. Seven drugs increase K,11.1 trafficking at clinically relevant concentrations.

Conclusion: We discovered clinically available drugs that could be readily tested as treatment for patients with Long QT Syndrome caused by trafficking deficient K,11.1 variants.

PO-616-04
A NOVEL CPVT-ASSOCIATED CALMODULIN MUTATION CAUSES SEVERE CA2⁺ LEAKAGE FROM SARCOPLASMATIC RETICULUM IN IPSC MODEL BY ACTIVATING THE CARDIAC RYANODINE RECEPTORS
Jingshan Gao; Takeru Makiyama; Yuta Yamamoto; Jingshan Gao; Hisaaki Aoki; Jingshan Gao; Jingshan Gao; Asami Kashiwa; Jingshan Gao; Jingshan Gao; Hirohiko Kohjitani; Jingshan Gao; Naomasa Makita; Jingshan Gao; Jingshan Gao; Seiko Ohno; Jingshan Gao; Jingshan Gao; Minoru Horie and Jingshan Gao

Background: The potassium channel K,11.1 plays an important role in repolarization of cardiac action potentials and loss-of-function (LOF) K,11.1 variants cause Long QT Syndrome which predisposes individuals to fatal cardiac arrhythmias. About 90% of LOF mutations prevent K,11.1 intracellular transport (trafficking) to the plasma membrane and prolonged incubation with drugs can sometimes increase K,11.1 trafficking and restore K,11.1 current (I,K,11.1).

Objective: Develop an optimized thallium (Tl⁺)-flux assay to screen a library of clinically approved drugs for increased trafficking of two K,11.1 potassium channel variants.

Methods: We developed a novel Tl⁺-based fluorescent assay and HEK-293 cells expressing K,11.1 trafficking-deficient variants (K,11.1-G601S-G965*X and K,11.1-N470D) to screen 1900 drugs (three replicates each) for increased K,11.1 trafficking. HEK-293 cells were plated on 384-well clear bottomed plates with 10 μM drug in individual wells 24-hours before experiments. On the day of experiments, drug was washed out, loaded with thallium-sensitive dye, and imaged using a 384-well fluorescent plate reader. Drug hits were detected using the slope of fluorescence in the assay and calculating the median and median absolute deviation (MAD).

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Conclusion: We discovered clinically available drugs that could be readily tested as treatment for patients with Long QT Syndrome caused by trafficking deficient K,11.1 variants.