Objective: To obtain APD and CV restitution curves from explanted human hearts with optical mapping, and take advantage of the experimental data to refine the dynamics of an ionic model, which can be valuable for arrhythmia simulation studies.

Methods: Optical mapping of membrane potentials was performed on explanted human hearts (n=2 from recipient patients and n=1 from a rejected donor) at high resolutions (256x256 pixels, at 500 Hz) and a large field of view of 8 x 8 cm². Action potential was measured across the anterior epicardial RV and LV and the endocardium LV, paced at CLs from 3 sec and shorter, until conduction block or VF induction. APD and CV restitution were obtained across the mapped tissue.

Results: Optical voltage signals were obtained by pacing the heart at different CLs (Panel A). APDs and CVs were calculated, and restitution curves for APD and CV were calculated for different regions in the hearts. APD alternans, between even and odd beats, were observed and quantified (panels B and C). A human ventricular cardiomyocyte model was fitted to the experimentally obtained APD and CV restitution curves to reproduce AP duration (APD restitution) and conduction velocity (CV restitution) at all CLs. The resultant ionic model recapitulates the experimental data including the bifurcation period and magnitude of alternans as well as the wave propagations.

Conclusion: Optical mapping of action potential from explanted human hearts were used to refine the dynamics of an ionic model of human ventricular myocytes. The refined model reproduced the experimental wave propagations at all CLs, including alternans. Our study presents a clinically relevant in silico model to study the induction and dynamics of arrhythmias in whole heart simulations.

BS-516-04

ULTRASTRUCTURAL AND MOLECULAR ORGANIZATION DETERMINE CONDUCTION DIFFERENCES BETWEEN IN ATRIAL AND VENTRICULAR WORKING MYOCARDIUM

Heather Struckman MS; Nicole Moise MD; Celine Dagher BS; Zhenhui Chen PhD; Seth H. Weinberg PhD and Rengasayee Veeraraghavan PhD

Background: The intercalated disc (ID) is a complex, heterogeneous structure that provides electrical (gap junctions; GJ) and mechanical (adherens junctions [AJ], desmosomes [Des]) coupling between cardiomyocytes. ID-localized populations of electrogenic proteins responsible for the action potential upstroke - cardiac sodium channels [NaV1.5], inward-rectifier potassium channels [Kir2.1] and sodium potassium ATPase [NKA] - are vital machinery for cardiac impulse propagation. Thus, ID nanostructure is emerging as a critical determinant of cardiac conduction and nanoscale ID damage has been linked to arrhythmia in human patients.

Objective: To determine differences between ultrastructure and molecular organization in atrial and ventricular working myocardium.

Methods: Transmission electron microscopy (TEM), sub-diffraction confocal imaging, stochastic optical reconstruction microscopy (STORM), 3D finite-element modeling, multiscale computational modeling

Results: TEM revealed structural differences from the micro- through nano-scales including key factors that may underlie faster atrial conduction: more numerous GJs with associated perinexi and reduced intermembrane spacing (similar findings at MJs). Confocal microscopy revealed ID enrichment of NaV1.5, Kir2.1 and NKA with more intense immunosignals at the ID vs
non-ID regions in atrial myocytes than ventricular. STORM defined the NaV1.5, Kᵢ2.1 and NKA distribution relative to the junctions: In the ventricle, NaV1.5 associated most closely with GJ (median intercluster distance: 117 nm), Kᵢ2.1 with Des (151 nm), and NKA with both GJ (165 nm) and AJ (150 nm). Next, percent of each electrogenic protein localized within 100 nm from ID junctions: 35% of NaV1.5 around GJs, 49% of Kᵢ2.1 around Des and 33% and 39% of NKA near GJ and AJ respectively. Protein organization within atria ID had some notable differences: NaV1.5, Kᵢ2.1 and NKA was shifted closer to GJs, NaV1.5 to Des, and Kᵢ2.1 and NKA to Ncad.

**Conclusion:** These data provide the first-ever comprehensive quantitative picture of ID ultrastructure and molecular organization. Functional implications of these nanoscale structural differences will be elucidated by implementation into our recently published 3D finite-element computational model.

**ABSTRACT CE-543:**
The Early the Better: Afib Detection and Stroke

**Sunday, May 1, 2022**
10:30 AM - 11:30 AM

**CE-543-01**

4-FOLD HIGHER RATE OF ATRIAL FIBRILLATION DETECTION AFTER STROKE OF PRESUMED KNOWN ETIOLOGY WITH CONTINUOUS VERSUS INTERMITTENT MONITORING: RESULTS FROM THE STROKE AF STUDY

Jonathan P. Piccini MD, MHS, FHRS; Christopher Granger; Richard A. Bernstein MD, PhD; Hooman Kamel; Jeffrey Katz; pramod P. sethi MD; Evgeny Sidorov MD; Scott E. Kasner MD; Scott B. Silverman MD; Theodore Merriam MS; Paul Ziegler MS and Lee Schwamm MD

**Background:** In patients (pts) with recent ischemic stroke, atrial fibrillation (AF) may be common regardless of the stroke etiology. Timely diagnosis and intervention may prevent more disabling recurrent strokes.

**Objective:** We sought to compare incidence rates of AF, defined as an episode ≥ 2 minutes, between various intermittent monitoring strategies vs continuous monitoring with an insertable cardiac monitor (ICM) in pts with strokes attributed to large artery atherosclerosis (LAA) or small vessel occlusion (SVO).

**Methods:** The STROKE AF study enrolled pts with a recent ischemic stroke attributed to LAA or SVO. Included pts were ≥60 years old (or 50-59 with heart failure, hypertension, diabetes, prior stroke, or vascular disease) and had no history of AF. One-time monitoring strategies were simulated by computing the AF incidence using 1, 2, 7, 14, and 30-day recording periods. Repeated monitoring strategies (quarterly 24 h, 48 h, 7d, or monthly 24 h) were simulated over a 1-year period. The initial day for all simulations was randomly selected 1-14 days after ICM placement from a uniform distribution. Repeated monitoring strategies were simulated with mean values and ranges reported.

**Results:** We obtained data from 242 pts (age 66.6±9.3, 60% male, CHA₂DS₂-VASc 5.0 [IQR4.0-5.0]). The AF incidence rate via ICM at 12 months was 11.57%, exceeding the estimated rates from all forms of modeled intermittent monitoring (range 0.22-2.55%, p<0.001, Figure). The AF incidence rate via ICM at 12 months was 11.57%, exceeding the estimated rates from all forms of modeled intermittent monitoring (range 0.22-2.55%, p<0.001, Figure).

**Conclusion:** In the vast majority of LAA/SVO stroke pts, AF detected via ICMs would go undetected via conventional intermittent monitoring strategies and therefore these pts may not be optimally managed for recurrent stroke prevention.