characteristics were collected including procedure time, fluoroscopy use and electrical parameters.

**Results:** A total of 72 CSP implants were performed with a variety of pacing configurations including HBP (35), His optimised-CRT (2), LBP (34) and left bundle optimised-CRT (1). Implants were a mixture of de-novo implants (67) and device upgrades (5). During the study period there was a transition from HBP to LBP (Figure 1). Back-up leads were placed in 29% (10) of HBP systems, none were required in LBP systems. R-waves were larger (12.3 vs 3.2mV, \( p<0.01 \)) and capture thresholds lower (0.68 @ 0.4/0.5ms vs 1.32 @1ms, \( p<0.01 \)) with LBP. Intrinsic QRS duration was similar between the two groups (135 vs 120ms, \( p=0.3 \)). LBP resulted in a significant shortening of QRS duration (135 vs 111ms, \( p<0.01 \)) and HBP resulted in a non-significant shortening of QRS duration (130 vs 118ms, \( p=0.22 \)) (Figure 2). Procedure times were shorter for LBP compared to HBP (88 vs 106min, \( p=0.03 \)). The only complication was 1 haematoma not requiring intervention following a HBP implant; there were no lead dislodgements.

**Conclusion:** Our early experience of CSP shows that the implant procedure is shorter and electrical parameters better with LBP compared to HBP. There was a switch from HBP to LBP over the period studied. Both are viable, safe techniques in a centre establishing a CSP program.

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**Figure 1. Trend in HBP and LBP over the study period.**

**Figure 2. Change in QRS duration with His bundle pacing and left bundle branch pacing compared to intrinsic QRS duration (black dashed line represents the mean values).**

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**PO-614-08**

**SODIUM CHANNEL Na\(_{v}\)1.6 AND NA-CA EXCHANGER REMODELING CONTRIBUTES TO ARRHYTHMOGENIC LATE SODIUM CURRENT AND Ca\(_{2+}\) SPARKS IN THE PRESENCE OF D96V MUTANT CALMODULIN**

Heather Struckman; Mikhail Tarasov; Yusuf Olgr; Sandor Gyorky PhD; Rengasayee Veeraraghavan PhD and Przemyslaw Radwanski PharmD, PhD

**Background:** Calmodulin (CaM) facilitates sodium channel (Na\(_{v}\)) inactivation, thereby preventing proarrhythmic late sodium current (I\(_{Na}\)). To date, a link between arrhythmogenic mutations in CaM and Na\(_{v}\) dysfunction is not well established. Outside of Na\(_{v}\)1.5, dysfunctional inactivation of Nav1.6 promotes late I\(_{Na}\*)-mediated arrhythmias.

**Objective:** Investigate Nav1.6 dysregulation by arrhythmogenic calmodulin (CaM) mutant D96V.

**Methods:** Nav1.6-expressing CHO cells, transgenic mice, super-resolution microscopy (sub-diffraction confocal imaging [sDCI], STED, STORM), scanning ion conductance microscopy (SICM)-guided “smart” patch clamp.

**Results:** STED revealed enlarged Na\(_{v}\)1.6 clusters in CHO cells transfected with D96V-CaM compared to WT-CaM. In transgenic mice with cardiac-specific D96V-CaM expression (cD96V), sDCI revealed D96V-CaM distributed in a striated pattern (consistent with T-tubular localization) along with ryanodine receptor (RyR2). Na\(_{v}\)1.6 clustering was quantified with STORM: In both WT and cD96V hearts, \( \approx 50\% \) of Na\(_{v}\)1.6 clusters localized \(<100\text{nm} \) from RyR2. Intriguingly, Na\(_{v}\)1.6 density within these regions increased 67\% in D96V relative to WT. The functional consequences of this structural Na\(_{v}\)1.6 remodeling was assessed with SICM-guided “smart” patch allowing for the recording of Na\(_{v}\) activity localized at T-tubule openings. D96V myocytes displayed increased cluster size and frequency of late Na\(_{v}\)1.6 burst openings. Previous studies have implicated such aberrant late Na\(_{v}\) activity in proarrhythmic Ca\(_{2+}\) mishandling. To assess the potential for such, we investigated sodium-calcium exchanger (NCX) localization near Na\(_{v}\)1.6. STORM revealed that 77\% of Nav1.6 clusters localized \(<100\text{nm} \) from NCX in WT compared to 89\% in D96V hearts. Nav1.6 density within these regions increased 48\% in D96V relative to WT. Interestingly, NCX cluster density was preferentially increased near Nav1.6 in D96V hearts. In functional imaging studies, D96V myocytes displayed larger, more frequent Ca\(_{2+}\) sparks relative to WT which was reversed by cardiac-specific Na\(_{v}\)1.6 knockout.

**Conclusion:** To our knowledge, this is the first report of proarrhythmic cardiac structural remodeling secondary to a CaM defect, providing mechanistic insight into calmodulinopathy.

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**POSTER PO-615:**

**Featured Posters: Allied Professionals and Basic Science at Pod 2**

Friday, April 29, 2022
12:30 PM - 2:30 PM

**PO-615-01**

**ROLE OF KCNQ1 REGULATION IN VARIABILITY IN ACTION POTENTIAL PROLONGATION BY IKR BLOCK**

Yuko Wada MD, PhD; Lili Wang PhD; Lynn D. Hall; Laura L. Short; Ashli E. Chew MS; Joseph F. Solus PhD and Dan M. Roden MD, FHRS

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