ABSTRACTS

ABSTRACT AB01:
Teaching Case Abstracts

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB01-01

SINUS NODE DYSFUNCTION: AN UNCOMMON COMPLICATION OF LEFT SIDED FLUTTER ABLATION

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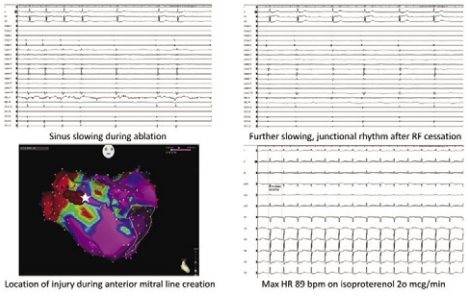
Introduction: Left sided ablation may lead to thermal injury of the arterial network which supplies the sinus node (up to 45% of the population), resulting in profound sinus bradycardia and arrest. We present a case of sinus node dysfunction following ablation of a left sided atrial flutter originating anterior to the right sided PV's.
Methods: N/A
Results: A 75 year old woman with a structurally normal heart and drug refractory AFib, typical right sided flutter and left sided flutter despite prior ablations was referred to our institution for re-do ablation. Baseline EP measurements were normal and a CTI line was created with bidirectional block. Catheters were advanced into the LA to address the PV's and left sided flutter. Programmed stimulation induced a perimitral flutter (CL 240 ms) matching her clinical arrhythmia which was ablated using an anterior line (RSPV-MVA). After placing a single lesion, she had a sudden and profound decrease in heart rate requiring CS pacing. The right sided PV's remained chronically isolated and the left sided PV's were re-isolated. With isoproterenol (20 mcg), the sinus rate increased to ~ 100 bpm, but with cessation, severe sinus node dysfunction remained. As such, a dual chamber PPM was placed.
Conclusions: Sinus node dysfunction resulting from thermal injury during left sided ablation is a serious issue resulting in the need for permanent pacing. Consideration of pre-ablation imaging to visualize the arterial supply as well as using an inferior line (LIPV-MVA) may be reasonable precautions.



AB01-02

DEFIBRILLATION THRESHOLD TESTING TO GUIDE MANAGEMENT IN PATIENTS WITH A CONTINUOUS FLOW LEFT VENTRICULAR ASSIST DEVICE

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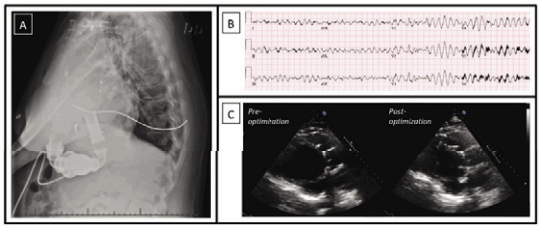
Introduction: While the utility of defibrillation threshold (DFT) testing at initial ICD implant is debated, placement of a left ventricular assist device (LVAD) may compromise ICD function. We present a series of LVAD patients for whom formal DFT testing was used to guide management.
Methods: N/A
Results: Patient 1: 47-year-old man with dilated cardiomyopathy (CM), status post HeartMate 2 (HM2) LVAD. Given syncope and documented non-sustained VT, an ICD was implanted post-LVAD. Initial DFT was >35J despite optimal lead placement. A subcutaneous defibrillator coil was implanted, with subsequent DFT ≤ 20J (Fig 1a). Patient 2: 56-year-old man with ischemic CM, status post ICD implant and HeartWare HVAD 6 years later. At ICD generator change, DFT testing was deferred. He later presented in VF with ineffective ICD shocks (Fig 1b). After hemodynamic optimization, DFT remained greater than maximum programmable ICD output. He underwent VT ablation and addition of a subcutaneous coil. Post-revision DFT was ≤ 36J. Patient 3: 72-year-old man with dilated CM, status post BiV-ICD and HM2 LVAD. He presented with ineffective ICD shocks for sustained VT. Echocardiography showed severe LV dilatation, with left ventricular end-diastolic dimension (LVEDD) 8.5 cm. After diuresis and LVAD optimization via hemodynamic ramp study, LVEDD was 6.8 cm (Fig 1c). Subsequent DFT was ≤ 30J, and no device revision was pursued.
Conclusions: These cases highlight the need for a multidisciplinary approach to the management of ICDs in LVAD patients. Device reprogramming and/or revision when appropriate may reduce both shock burden and morbidity, and DFT testing can influence clinical decision-making.



AB01-03

LEFT ATRIAL DIVERTICULUMS AS THE SITE OF FOCAL ATRIAL TACHYCARDIAS

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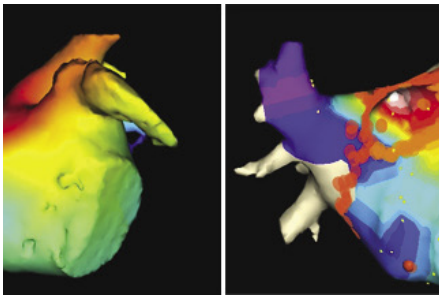
Introduction: Forty-six percent of patients undergoing AF ablation have a left atrial diverticula. Caution is required when ablating near these structures to avoid perforation. While considered an impediment to ablation, an arrhythmogenic role of this structure has not previously been described. We report 2 cases of focal atrial tachycardia (AT) arising from an anterior LA diverticulum.
Methods: N/A
Results: A 75yo female presented with recurrent AT (CL 270ms) after previous AF ablation involving pulmonary vein isolation. CT showed a diverticulum anterior to the RSPV. Entrainment excluded a peri-mitral or cavo-tricuspid macro re-entrant tachycardia. Electro-anatomic mapping showed equal activation at the septal RA-SVC junction and the anterior base of the LAA (left image). Mapping of the region between these sites demonstrated early activation at the tip of the diverticulum. Ablation was performed at the roof and anterior to the diverticulum, successfully isolating the structure and terminating

the tachycardia. A 49yo male with persistent AF presented for ablation. During isolation of the posterior LA, AF terminated to AT (CL 260ms) with alternating coronary sinus (CS) activation. Activation mapping of the RA, LA and CS demonstrated the anterior diverticulum as the earliest site (right image). Ablation anterior to the structure isolated the diverticulum and terminated the tachycardia to typical atrial flutter. A cavo-tricuspid isthmus ablation restored the patient to SR.
Conclusions: Left atrial diverticula are frequently observed. These cases demonstrate AT originating deep within a left atrial anterior diverticulum; implicating these structures in atrial arrhythmogenesis.



AB01-04

SAVED BY AN LVAD: SUSTAINED RAPID VENTRICULAR TACHYCARDIA MISCLASSIFIED AS SVT IN THE VENTRICULAR FIBRILLATION ZONE

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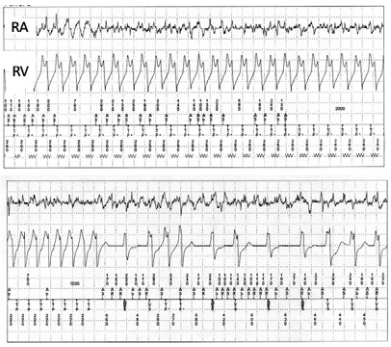
Introduction: Inappropriate ICD therapies are linked to adverse clinical outcomes and recent large multicenter studies have provided supporting evidence for the safety of programming long VT detection times and programming rapid tachycardia discrimination on in the VF zone. False negative VT discrimination in the slower VT zones has been described but inappropriate VT discrimination in the rapid VT/VF zone has not been reported.
Methods: N/A
Results: 68 year old Caucasian male with history of end stage ischemic cardiomyopathy, prior VT and s/p LVAD placement was seen for routine ICD follow-up (Medtronic Protecta XT- CRT-D D314TRG; tachycardia zones: VF 194 bpm 30/40 intervals, and FVT via VF 194-250 bpm, VT:167bpm 76 intervals. PR Logic on, Wavelet is on 76%, stability and onset off, SVT limit 250 bpm, high rate timeout off). Device log-book showed multiple episodes of VTs terminated by ATP and three SVT episodes up to 46 min duration. Representative VT and SVT episodes are shown in the Figure. There is atrial fibrillation with a rapid regular ventricular rhythm (222 bpm). The VT event was falsely classified as SVT due to morphology match (WV-in top panel) and continued for 46 min. Eventually the episode was reclassified and terminated with an ATP. It is likely that the morphology template update algorithm chose a PVC beat for baseline.
Conclusions: For the first time we have shown that tachycardia discriminators may misclassify very rapid ventricular arrhythmias. These events may be underreported.



AB01-05

THE CALM BEFORE THE STORM: TIME COURSE AND IMAGING PRECURSORS FOR IDENTIFICATION OF AN ATRIOESOPHAGEAL FISTULA FOLLOWING CATHETER ABLATION OF ATRIAL FIBRILLATION

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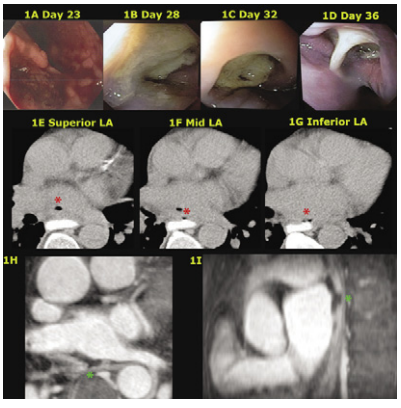
Introduction: Atrioesophageal fistula is a dreaded complication of atrial fibrillation (AF) with little warning prior to presentation. We present the time course and imaging findings of an atrioesophageal fistula prior to presentation with a transient ischemic attack and septic shock.
Methods: N/A
Results: A 69 year old male underwent catheter ablation for AF at an outside institution. One day post-ablation he experienced odynophagia; 23 days post-ablation, he had hematemesis with hypovolemic shock. Endoscopy identified a bleeding esophageal ulcer (Figure 1A); a CT scan identified air bubbles (*) between the posterior LA and esophagus (Figure 1E, 1F, 1G). On day 30, a cardiac MRI identified an anterior esophageal erosion (*) adjacent to the posterior LA (Figure 1H, 1I). Serial endoscopies showed a persistent esophageal ulcer (Figure 1B, 1C, 1D). Forty days post-ablation the patient developed septic shock with left hemiparesis. A brain MRI identified a right cerebral air embolus. Emergent repair of the atrial perforation and esophageal ulcer was performed. On day 57, the patient underwent esophagectomy for an esophageal leak; an esophageal reconstruction was performed 9 months post-ablation. Fourteen months post ablation, the patient has made a full recovery.
Conclusions: Atrioesophageal fistula is a potentially fatal complication of AF ablation. Early detection and intervention is crucial to avoid stroke and death. This case highlights serial imaging findings of an atrioesophageal fistula post ablation. If any of the corresponding imaging findings are noted, emergent surgical repair is recommended to avoid catastrophic complications.



AB01-06

IMPROVED WORKFLOW FOR CIED REMOTE MONITORING MANAGEMENT: A QUANTITATIVE STUDY

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Introduction: The volume of patients (pts) enrolled in remote monitoring (RM) has increased greatly in recent years. Device clinics are responsible for reviewing the recurring influx of RM data, but there is a paucity of data on time aspects for the entire review process. We aimed to collect RM workflow metrics and improve efficiency and quality in a device clinic that follows over 5,000 CIED pts on RM.
Methods: First, detailed process flow maps were created to document each step of the RM process. Next, key steps were time-recorded for each remote: starting at receipt (R) into the RM system to completed nurse documentation (ND), and also to completed physician signature (PS). Full lead time (LT) was the entire process from R to PS. All RM manufacturer systems were included and remotes were coded as scheduled, unscheduled, or alert. After baseline metrics were collected over 2 weeks, the team identified inefficiencies and quality improvement opportunities; solutions were implemented. After 9 months, the same metrics were collected for all remotes over a 2-week period.
Results: A total of 159 remotes were received at baseline and 93 at final (6% loop recorder, 12% CRT, 36% pacemaker, 46% ICD). Workflow improvements included: a dedicated nurse for triaging of alert remotes in an interruption-free environment, post-triage distribution of routine remotes for review amongst in-clinic staff and phone triage nurses, aggressive management of repeat alerts via both protocols and clinical decision autonomy, and electronic messaging to physicians. Compared to baseline, final LT was 83% shorter, from mean 32.3 ± 6.8 days to 5.6 ± 2.8 days ($p<.001$) for all remotes. On average, R to ND decreased 77% from 10.3 ± 6.9 days to 2.4 ± 1.6 days ($p<.001$) and ND to PS time decreased 85% from 22.0 ± 30.7 days to 3.2 ± 2.4 days ($p<.001$). An unaltered process step was initial triage to separate urgent from routine remotes; LT for urgent ones was 1.0 day at baseline and remained unchanged at final. The percentage of non-scheduled remotes received, unscheduled or alert, decreased from 50% to 26%.
Conclusions: In this study where workflows and environment within a very large device clinic were revised to improve overall RM workflow, dramatic increases were observed in efficiency and quality.

ABSTRACT AB02: Mechanisms of Arrhythmias

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB02-01

ELECTROPHYSIOLOGICAL SUBSTRATE OF EARLY REPOLARIZATION SYNDROME IN HUMANS

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Introduction: Early repolarization syndrome (ERS) is associated with increased susceptibility to ventricular fibrillation and sudden cardiac death. The precise electrophysiological substrate of ERS and mechanisms of arrhythmia in humans are still unknown.
Methods: We characterized the electrophysiological properties of four human ventricles obtained through our university hospital organ donor program. One individual had documented ERS of the lateral left ventricle characterized by J-point elevation in leads I, II, and v4-6. High resolution optical mapping was used to image left ventricular wedge preparations perfused with DI-4-ANBDQBS voltage-sensitive dye. Activation time (AT), action potential duration (APD80) and repolarization time (RT) at 80% of repolarization were derived from endocardial maps. Action potential triangulation was determined as: (APD80-APD20)/APD80; and spatial dispersions as differences between 5 and 95% of frequency distributions.
Results: Pacing at 1Hz revealed significantly shorter APD80 in ERS (237.2±26.6 ms) compared to controls (314.2±21.6, 339.6±24.5, 397.1±33.9 ms; $P<0.05$). Similar trends were observed for RT (293.7±27.5 ms vs. 353.8±27.6, 393.4±24.8, 425.6±45.1 ms; $P<0.05$) and triangulation (0.48±0.04 vs. 0.50±0.04, 0.55±0.06, 0.49±0.06; $P<0.05$). However, at 2Hz, APD80 was decreased in controls but not in ERS. Nevertheless APD80 remained significantly shorter in ERS (235.3±32.4 vs. 256.4±17.0, 262.4±19.1, 313.1±17.4 ms; $P<0.05$). RT was shortened in controls (300.3±27.4, 322.4±29.8, 347.8±29.3 ms; $P<0.05$) yet prolonged in ERS (318.2±31.2 ms; $P<0.05$). This was attributed to significant prolongation of the total AT by 81.8%, compared to controls (13.9% 10.2% 31.1%). Moreover, ERS showed increased dispersions of APD80 (184.3 ms vs. 85.0, 105.7, 100.1 ms) and RT (161.9 ms vs. 103.7, 128.6, 113.8 ms) than in controls at 2Hz. Pacing ≥ 2Hz induced conduction alternans in ERS but not in controls. No evidence for augmented fibrosis or adiposis was found in ERS, as determined by histology and high resolution MRI.
Conclusions: This is the first detailed characterization of the electrophysiological substrate of ERS in human which was found to be associated with a combination of conduction and repolarization remodeling.

AB02-02

THE EFFECT OF SHORT LASTING ROTATING WAVES ON ATRIAL FIBRILLATION COMPLEXITY

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Electrophysiology, Hamburg, Germany

Introduction: Recent studies suggest rotors may contribute to perpetuation of atrial fibrillation (AF).
Methods: Mapping of electrical activity during AF was performed using high-density epicardial recordings of human paroxysmal or persistent AF (N=21 pts) with an array of 16x16 electrodes (1.5 mm electrode spacing) placed on the epicardial surface of the left atrial (LA) posterior wall and the right atrial (RA) free wall. Rotors were detected as phase singularity points with >1 rotation lifespan. Individual waves were reconstructed using template matching and clustering approach.
Results: Epicardial rotor mapping identified 138 rotors in total (0.36±0.35 rotors per s on average). All detected rotors had short lifespan with the longest of 585 ms (3.2 rotations). Rotors were present for 7.8±7.0% of the time (min: 0%, max: 26%). See Figure 1 for diagram representing periods of time rotors occurred and the area occupied by rotor. 74% of rotors appeared and disappeared within the mapped field. On average, 0.5±0.5% of fibrillatory waves in PAF group and 0.8±0.7% in PersAF group formed rotors. The AF cycle length was not different before, during and after rotor occurrence. The total number of fibrillation waves increased during rotor occurrence but afterwards went back to base level prior to the rotor occurrence (prior: 0.37±0.14, during: 0.44±0.17, after: 0.37±0.13 waves/AFCL/s; p<0.03).
Conclusions: Rotor identification using phase mapping of contact electrograms revealed their low incidence, short life span and lack of effect of their occurrence on AF cycle length and the AF complexity. Those findings suggest that short-lasting rotors may not play a critical role in AF maintenance.

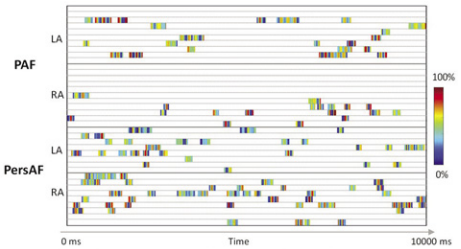

Figure 1 Incidence and area occupied by rotors (as percentage of mapped field). Each row represents an individual recording. White background denotes lack of rotor at given time point. Colored blocks represent periods of time rotor was present with a color denoting % area occupied by a rotor.

AB02-03

UNRAVELING KEY PATHOGENIC NETWORKS FOR HOW PLAKOPHILIN-2 (PKP2) MUTATIONS LEAD TO ABNORMAL PPARγ ACTIVATION AND ARVD PATHOLOGIES

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Introduction: Arrhythmogenic Right Ventricular Dysplasia (ARVD) is an inherited cardiomyopathy characterized by progressive fibrofatty replacement of CMs with increased CM apoptosis primarily in the RV, leading to lethal arrhythmia. We have established an in-vitro ARVD model using patient-specific induced pluripotent stem cells-derived CMs (iPSC-CMs) with PKP2 mutations. We first developed a three-factor (3F) protocol (steroid, insulin & IBMX) to induce metabolic maturation of primitive iPSC-CMs. We found that ARVD iPSC-CMs depicted ARVD pathologies only after inducing adult-like, PPARα-dependent metabolism (by 3F) and abnormal activation of PPARγ (by 5F = 3F + indomethacin & rosiglitazone), resulting in exaggerated CM lipogenesis and apoptosis. PPARγ antagonists could rescue ARVD pathologies but carry side effects (e.g. hypertension). Elucidating the mechanisms underlying how PKP2 mutations lead to abnormal PPARγ activation in ARVD CMs would enable developing novel therapies.
Methods: We generated iPSC-CMs from normal iPSCs or ARVD iPSCs with PKP2 c.2484C>T mutations. iPSC-CM cultures treated with 0F, 3F or 5F were studied by Western/Co-IP, immunostaining, microarrays and qPCR to elucidate key pathogenic networks mediating the abnormal PPARγ activation in ARVD CMs.
Results: We found that mutant PKP2 led to faster degradation of plakoglobin protein (Pkg)(76.1±1.8%, 68.4±1.1% & 51.3±6.8% of control CMs after 2.5 weeks of 0F, 3F, or 5F respectively, p<0.05 by ANOVA), which is the anchoring protein on the insulin receptor (InsR) for p85 of the PI3K pathway. With less available Pkg for p85 binding, insulin was less effective in activating PI3K via InsRs, leading to insulin resistance, less Akt activation, and hyperactive GSK3β that further decreased Yes-associated protein (YAP), β-catenin and Pkg activities. Downregulation of YAP and β-catenin led to decreased levels of a microRNA (miR) 24/27b cluster (inhibitory miRs for PPARγ) in ARVD CMs, allowing abnormal activation of PPARγ and ARVD pathologies.
Conclusions: PKP2 mutations lead to faster degradation of Pkg and subsequent insulin resistance with hyperactive GSK3β that reduces YAP and β-catenin activities, which downregulate a miR cluster allowing PPARγ over-activation and ARVD CM apoptosis.

AB02-04

PATHOLOGICAL INTERACTIONS OF ARVD CARDIOMYOCYTES (CMS) WITH ARVD MESENCHYMAL STROMAL CELLS (MSCS)

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Introduction: Arrhythmogenic Right Ventricular Dysplasia/ Cardiomyopathy (termed ARVD here) can cause sudden death in young adults. Pathological hallmarks of ARVD are progressive fibrofatty replacement of CMs with increased CM apoptosis primarily in the RV. We have established an in-vitro ARVD model using patient-specific induced pluripotent stem cells-derived CMs (iPSC-CMs) with plakophilin 2 (PKP2) mutations to recapitulate CM lipogenesis & apoptosis. We and others had shown that ARVD cardiac MSCs are very adipogenic, yet in vitro cocktails used to induce adipogenesis of MSCs include non-physiological factors. ARVD patients are not typically obese, suggesting that the local milieu in ARVD hearts plays a major role in abnormal adipogenesis.
Methods: We generated MSCs and CMs from normal iPSCs and two ARVD iPSC lines with PKP2 c.2484C>T or c.2013delC mutations. CM-MSC cocultures, cytokine arrays, immunostaining, and qPCR were used to elucidate CM-MSC interactions.
Results: With 3 factor (3F=steroid+insulin+IBMX) adipogenic media, ARVD iPSC-MSCs displayed accelerated adipogenesis vs. normal MSCs. ARVD iPSC-CMs were first treated with 0F, 3F (for maturation) or 5F [=3F+2 PPARγ agonists (indomethacin & rosiglitazone) for inducing CM apoptosis] for 2.5 weeks and then all factors were withdrawn before CM-MSC cocultures. Only pathological ARVD CMs treated with 5F but not primitive or mature iPSC-CMs could induce accelerated adipogenesis of

ARVD MSCs. Moreover, normal but not ARVD MSCs protected ARVD CMs from apoptosis. Culture media with pathological ARVD iPSC-CMs had increased sCD40L, insulin and brain natriuretic peptide (BNP), which are endogenous factors that induce robust adipogenesis (perilipin1+ cells) of ARVD MSCs in 7 days (92.6 ± 1.8% vs. 4.3 ± 4% in controls, $p<0.01$ by Student t). Importantly, endogenous 3F failed to induce adiponectin expression in ARVD MSCs but not in normal MSCs, explaining the lack of CM protection by ARVD MSCs.
Conclusions: Pathological ARVD iPSC-CMs induce robust adipogenesis of ARVD MSCs by raising local BNP, insulin, and sCD40L levels, but fail to induce adiponectin expression in ARVD MSCs and thus cannot "save" ARVD CMs from apoptosis. Both cell types are essential to model diseased ARVD hearts in vitro.

AB02-05

RNA STABILIZING PROTEIN HUR RESCUES THE DOWNREGULATED SODIUM CHANNEL IN HEART FAILURE

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Introduction: Sodium currents are downregulated in heart failure (HF), and this downregulation has been linked to increased risk of arrhythmia in HF patients. Therefore, block or rescue of the downregulation of the cardiac sodium channel (SCN5A) may be useful for HF-associated arrhythmia prevention or treatment. HuR, an RNA binding protein, has been shown to bind to AU-rich elements in the 3'UTR of its target mRNA and to protect mRNA from degradation. Cardiac sodium channel gene SCN5A mRNA contains AU-rich elements
within its 3' UTR. Therefore, we investigated whether overexpression of HuR could prevent sodium channel downregulation after myocardial infarction (MI).
Methods: Mouse HuR was cloned into an AAV vector downstream of the cardiac troponin (cTNT) promoter. AAV constructs were packaged in serotype 9, and the AAV-9 solutions carrying HuR were injected into the MI mouse via the right jugular vein two weeks after left anterior descending coronary artery occlusion. Two weeks after injection, mice hearts will be collected to determine the expression of HuR and SCN5A.
Results: Compared with the MI mice injected with control AAV, MI mice injected with AAV HuR overexpression constructs showed 119.2% increase of SCN5A expression by Western blot (0.99 ± 0.14 in control vs. 2.17 ± 0.05 in HuR treated mice, P=0.000). We further cloned the DNA fragment flanking the putative ARE sites of SCN5A 3'UTR into the pEGFP-SCN5A mammalian expression plasmid immediately downstream of the SCN5A open reading frame to create pGEFP-SCN5A-ARE construct. After co-transfecting this plasmid into HEK293 cells with or without HuR overexpression, sodium current density was measured by patch clamp. As expected, there was a significant 151% increase in peak currents in cells with HuR overexpression compared with in those without HuR overexpression. (P=0.00).
Conclusions: RNA binding protein HuR can rescue the downregulated SCN5A expression in HF. Overexpression of HuR also increased sodium currents. Therefore, manipulation of HuR expression may be a useful strategy to treat HF associated arrhythmias.

AB02-06

CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA, TYPE 3: AN AUTOSOMAL RECESSIVE INHERITED CARDIAC ARRHYTHMIA CAUSED BY NOVEL MUTATION IN THE TECRL GENE

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Introduction: Primary cardiac arrhythmias could be one of the important causes of sudden cardiac deaths (SCD) in children and adolescents. Mutations in cardiac channel and their ancillary protein encoding genes have frequently been described in primary cardiac arrhythmias. Of them, KCNQ1, KCNH2, SCN5A, RYR2, CASQ2, CALM1-2 are the important ones. The aim is to present a new type of Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) and elucidate its genetic etiology.
Methods: Two families described in this study originated from Sudan. The parents in both families are first-degree cousins. Seven of their 13 children presented with exertion-induced arrhythmias or SCD. Five children died following the arrhythmic event. In the surviving two children, an Implantable Converter Defibrillator (ICD) was implanted in one child while the other suffered severe brain damage. Whole exome sequencing was performed to explore the genetic defect. Patient-specific stem cell induced-cardiomyocytes (hiPSC-CM) were made to evaluate the functional phenotype.
Results: ECG showed polymorphic ventricular fibrillation and torsade de pointes. ECG at rest showed borderline prolonged QTc interval of 450 ms. ICD interrogation of one surviving child revealed an episode of ventricular tachycardia. All affected children were homozygous for a splice donor site mutation, c.331+1G>A in the TECRL (also annotated SRD5A2L2) gene on chromosome 4. iPSC derived cardiomyocytes demonstrated elevated diastolic Ca2+ concentration, action potential prolongation and adrenergic induced triggered activity. Antiarrhythmic medication flecainide significantly reduced the triggered activity.
Conclusions: CPVT type 3 is a novel malignant form of cardiac arrhythmia, caused by homozygous mutation in the TECRL gene. These findings have implications for diagnosis and treatment of inherited cardiac arrhythmias.

ABSTRACT AB03:
Novel Therapeutic Approaches for Cardiac Arrhythmias

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB03-01

GENE TRANSFER OF CALMODULIN ALLEVIATES VENTRICULAR ARRHYTHMIAS IN A CALSEQUESTRIN-ASSOCIATED MOUSE MODEL OF CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA

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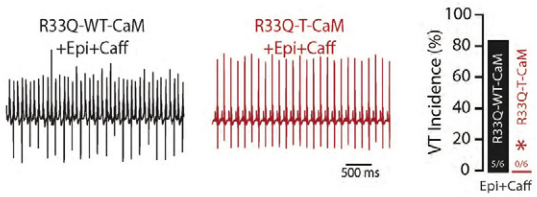
Introduction: Recent studies demonstrated that gene replacement utilizing adeno-associated virus (AAV) can rescue a CPVT phenotype associated with a mutated or absent cardiac-calsequestrin protein. However, virus based replacement-gene transfer is challenging for CPVT-associated mutations, as such replacement therapy can tackle only a subset of the CPVT disorders. Here we tested whether gene transfer of ubiquitous Ca2+-handling regulatory protein such as calmodulin, can serve as a general therapeutic avenue for CPVT mutations that predispose to aberrant Ca2+ release.
Methods: To that end, we have designed a therapeutic CaM (GSH-M37Q; T-CaM) which was delivered to adult mice (12 week of age) with a cardiac calsequestrin-associated CPVT mutation (R33Q) through AAV9. Eight weeks post-infection, we performed confocal microscopy to assess Ca2+ handling and recorded surface electrocardiograms to assess susceptibility to arrhythmias in vivo.
Results: During catecholamine stimulation with isoproterenol (Iso; 100 nM) T-CaM reduced Iso-promoted diastolic Ca2+ release (DCR) in isolated CPVT cardiomyocytes. Interestingly, such DCR reduction was not observed in cardiomyocytes that were isolated from CPVT mice treated with a wild type-CaM. Importantly, T-CaM exposure abolished ventricular tachycardia in CPVT mice undergoing epinephrine and caffeine challenge, which was not evidenced in wild type-CaM treated CPVT mice.
Conclusions: Our results suggest that gene transfer of T-CaM by AAV9 alleviates arrhythmias in a calsequestrin-associated CPVT model, thus supporting the potential of a CaM-based antiarrhythmic approach as a general therapeutic avenue for management of CPVT.



AB03-02

EFFICACY OF FLECAINIDE IN A LARGE COHORT OF PATIENTS WITH CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA

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Introduction: Some patients with catecholaminergic polymorphic ventricular tachycardia (CPVT) have significant ventricular arrhythmias (VA) or breakthrough cardiac events (BCE) despite β-blocker therapy. Based on reduction of exercise-induced VA burden and BCE rates during short-term follow-up in small studies, current guidelines recommend adding flecainide in these patients. We report the mid-term efficacy of flecainide in a large cohort of CPVT patients.
Methods: We included all patients with a clinical and/or genetic diagnosis of CPVT from 15 centers in whom flecainide had been initiated. We collected follow-up data on BCEs and compared the most recent exercise test on flecainide with the last exercise test before flecainide was initiated. Severity of VAs during exericse testing was scored as 0 points for no VA, 1 point for single ventricular extrasystoles, 2 points for bigeminy, 3 points for couplets, and 4 points for ventricular tachycardia.
Results: One-hundred-forty-four CPVT patients on flecainide therapy (median age 25.3 years, IQR: 16.3-39.5; 59% female; 58% proband) were included. Daily median flecainide dose was 2.0 mg/kg body weight (IQR: 1.6-3.0), and 124 (86%) patients also received β-blockers. Median follow-up durations from CPVT diagnosis to initiation of flecainide and on flecainide were 43 months (IQR: 3.5-95.5) and 37 months (IQR: 17.1-61.6), respectively. Among 22 patients who experienced a BCE on the highest tolerable β-blocker dose, 6 (26%) experienced a recurrent BCE after the initiation of flecainide ($p<0.01$). Mean annual BCE rate decreased significantly in this subgroup of symptomatic patients on β-blocker therapy ($p=0.02$). The VA score decreased in 64/89 (72%) patients with an exercise test before and on flecainide and remained equal in 17 (19%) patients ($P<0.001$). The number of patients with severe VAs (i.e. couplet or VT) decreased from 66 (62%) to 16 (15.8%) ($p<0.01$).
Conclusions: Flecainide was associated with a reduction in BCEs and ventricular arrhythmia burden in a large cohort of CPVT patients. These findings further support flecainide as a useful concomitant therapy in patients who are insufficiently controlled by β-blocker therapy alone.

AB03-03

ROLE OF NA+/CA2+ EXCHANGER (NCX) IN CARDIAC AUTOMATICITY AND VENTRICULAR REPOLARIZATION ASSESSED BY ORM-10962, A NOVEL HIGHLY SELECTIVE NCX INHIBITOR

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Introduction: The sodium-calcium exchanger (NCX) is considered as a major contributor to the maintenance of the intracellular Ca2+ homeostasis Since NCX is electrogenic ion-

transport system, it carries depolarizing and/or repolarizing ion currents, which influence cardiac action potentials (AP), however its contribution to the cardiac repolarization and automaticity has not yet been directly studied due to the lack of specific inhibitors.
Methods: The effects of a novel NCX inhibitor ORM-10962, was analysed in dog ventricular myocytes and in tissue preparations by applying the conventional microelectrode and whole cell patch-clamp techniques at 37 °C.
Results: ORM-10962 inhibited forward and reverse modes of NCX with estimated EC50 values of 54 nM, and 68 nM, respectively. This blocking effect of ORM-10962 was proved to be highly selective, since the drug even at the high concentration of 1 μM, did not affect late sodium current, calcium current, Na/K pump, rapid and slow delayed rectifier, transient outward and inward rectifier potassium currents. NCX blockade did not affect the amplitude of Ca2+ transients in left ventricular myocytes. In midmyocardial cells NCX inhibition by 0.5 and 1 μM ORM-10962 marginally shortened AP, in subepicardial cells and tissue moderately lengthened repolarization, while in subendocardial cells and intact Purkinje strands it did not elicit consistent AP changes. NCX inhibition induced negative shift of the plateau when forward mode of NCX was augmented and repolarization lengthening when reverse mode of NCX was favoured. ORM-10962 slowed automaticity in Purkinje fibres and sinus node in rabbits and dogs. In cardiac ventricular preparation in which the repolarization reserve was greatly attenuated by 100 nM dofetilide additional NCX inhibition by ORM-10962 did not change repolarization significantly.
Conclusions: NCX current plays a moderate role in cardiac automaticity and ventricular repolarization in normal ventricular muscle, which also depends on the relative magnitude of the forward and reverse mode of NCX. NCX inhibition may have antiarrhythmic effects by eliminating triggers for cardiac arrhythmia development and its influence on the arrhythmia substrate seems less important.

AB03-04

BLOCKING OF NAV1.8 CHANNEL IN LEFT STELLATE GANGLION SUPPRESSES THE VENTRICULAR ARRHYTHMIAS INDUCED BY ACUTE ISCHEMIA

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Introduction: Previous studies indicate that blocking of SCN10A/NaV1.8 could decrease neuron activity, and left stellate ganglion (LSG) hyperactivity promotes ventricular arrhythmias (VAs) induced by acute ischemia. The present study aims to investigate whether blocking of Nav1.8 with A-803467 in the LSG could decrease the incidence of VAs through suppressing LSG neuron activity.
Methods: Forty canines were averagely and randomly divided into dimethylsulfoxide (DMSO, Control) group, 10mM (low concentration), 15mM (moderate concentration) and 20mM (high concentration) A-803467 group. A final volume of 0.5ml A-803467 or DMSO was microinjected into the LSG. Ventricular effective refractory period (ERP), monophasic action potentials (MAPs), LSG function measured by relative maximal systolic blood pressure (SBP) increase in response to LSG stimulation, and LSG activity recorded by in vivo neural recording were measured. After 30 minutes A-803467 microinjection, acute ischemia was induced through occlusion of left anterior descending branch (LAD) for 1hour.
Results: There was no difference for heart rate or SBP at 30min after administration of A-803467 or DMSO when compared with baseline. However, a concentration -dependent prolonged ERP, APD70 and APD90 were identified after A-803467 treatment. Also, decreased LSG function and LSG neuron activity were observed in the A-803467 groups. More importantly, increased LSG neural activity induced by ischemia in the control group was significantly attenuated in the A-803467 groups and VAs were significantly reduced in the A-803467 groups.
Conclusions: Blocking of Nav1.8 channel with A-803467 attenuated VAs induced by acute ischemia, mainly through suppressing LSG neuron activity.

AB03-05

DANTROLENE PREVENTS ATRIAL FIBRILLATION INDUCTION IN A TACHYCARDIA-REMODELED SUBSTRATE BY STABILIZING RYANODINE RECEPTORS

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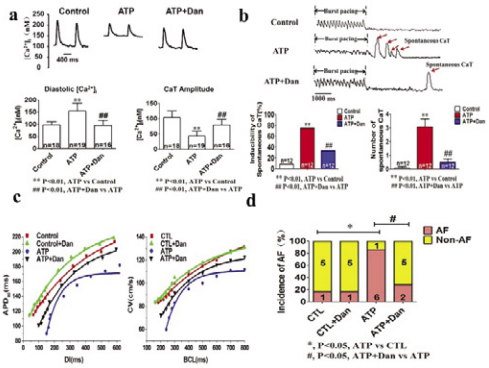
Introduction: Studies suggest a role for Ca2+ leak via ryanodine receptors (RyRs) in AF related remodeling. Dantrolene (DTL) is used clinically to treat malignant hyperthermia by stabilizing RyRs. Here we investigated the effects of DTL on atrial Ca2+ handling and AF inducibility in 7-day atrial tachypaced (ATP) dogs.
Methods: Electrophysiological study and optical mapping were performed before and after DTL administration in 6 control and 7 ATP dogs. Ca2+ transients (CaTs) were recorded with Indo 1 AM in LA cardiomyocytes (CMs) isolated from 5 CTL and 5 ATP dogs.
Results: ATP increased CM diastolic [Ca2+i] and reduced CaT amplitude (Fig A); DTL attenuated these abnormalities. Spontaneous Ca2+i release events were greatly enhanced in ATP CMs (Fig B), an effect suppressed by DTL. ATP prolonged RyR refractoriness, increasing basic cycle length (BCL) thresholds for CaT alternans, an effect reversed by DTL. Optical mapping of atrial preparations showed that despite reducing both ERP and APD, ATP increased the BCL threshold for CaT alternans and associated APD alternans (from 160±18 ms to 229±25 ms, $P<0.01$), steepened APD and conduction velocity (CV) restitution curves (Fig C) and promoted AF induction (86% in ATP vs 17% in CTL dogs, $P<0.01$). Dantrolene prolonged ERP and APD, yet decreased the APD alternans threshold (from 229±25 to 184±4 ms), flattened APD and CV restitution curves and prevented AF induction (Fig D). In vivo, ATP increased AF duration from 11±7 (CTL) to 585±210 s, $P<0.05$; DTL reduced AF duration in ATP dogs to 44±24 s.
Conclusions: DTL suppresses ATP-induced RyR dysfunction, thereby reversing the AF vulnerability caused by ATP induced remodeling.



AB03-06

THE ROLE OF ENDOTHELIN-RECEPTOR BLOCKADE IN THE PREVENTION OF THE SUBSTRATE FOR ATRIAL FIBRILLATION - AN INTERVENTIONAL STUDY IN AN OBESE OVINE MODEL

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Introduction: Endothelin-1 has been implicated in the pathogenesis of atrial fibrillation (AF), with upregulation of endothelin receptors in atrial tissue following weight gain. We hypothesised that direct inhibition with an endothelin receptor antagonist (ERA) would prevent the substrate for AF.
Methods: Obesity was induced in 20 sheep over 60 weeks using a high-calorie diet. Animals were randomized in equal groups to be: 1. treated with an ERA (bosentan, oral, 125mg bd) during this period; or 2. as controls. Endocardial EP studies and CMR were performed at 0, 30 and 60 weeks to determine conduction velocity (CV), refractoriness (ERP), AF inducibility and cardiac structure. Following terminal epicardial EP studies, atrial tissue was harvested to determine the degree of fibrosis and protein expression.
Results: See table. At 60 weeks, the following were observed with ERA treatment compared to obese controls: improved conduction velocity (1.15 vs 0.94m/s p<0.001); no difference in ERP or atrial voltage; reduced fractionation (17.7 vs 26.0% p=0.05); less AF induced (52.5 vs 77.5% p=0.04) and shorter AF episodes (20.5 vs 47.0s p=0.04); reduction in atrial fibrosis (3.8 vs 6.0% p=0.02); increased connexin-43 expression (p=0.01); and reduced expression of AngII (p=0.05), CTGF (p=0.003) and IL-6 (p=0.02).
Conclusions: Intervention with an endothelin receptor antagonist prevented atrial electrical remodelling due to obesity. In particular, there was attenuation of conduction slowing, reduction in AF burden and inhibition of atrial fibrosis and inflammation. This may represent a unique therapeutic target in AF associated with obesity.

Table 1. Comparison of ERA treated and control animals at 60 weeks

Variable	ERA treated (n=10)	Obese Control (n=10)	p value
Weight (kg) Body fat (%)	95±9 43±4	92±7 41±5	NS NS
Systolic BP (mmHg) LAP (mmHg) LA volume (ml) LVEF (%)	89±10 6.7±1.4 55.5±13.9 49±6	90±11 6.8±1.8 50.5±9.1 47±8	NS NS NS NS
LA voltage (mV) Fractionation (%) ERP 400 (ms)	5.81±0.31 17.7±8.2 180±19	5.77±0.36 26.0±9.0 181±17	NS 0.05 NS
Endocardial CV (m/s) Epicardial CV (m/s) Heterogeneity	1.15±0.11 0.98±0.03 1.28±0.05	0.94±0.06 0.92±0.03 1.47±0.05	<0.001 0.001 0.02
AF inducibility (%) AF duration (s)	52.5±23.8 20.5 [IQR 38.2]	77.5±19.8 47.0 [IQR 93.0]	0.04 0.04
Atrial fibrosis (%) Connexin 43 (%)	3.8±1.7 2.8±0.7	6.0±1.5 1.9±0.5	0.02 0.01
Atrial protein expression (%):			
TGF-β AngII CTGF IL-6	2.2±0.6 0.6±0.1 0.9±0.3 1.9±1.1	2.2±0.9 0.8±0.2 1.6±0.4 3.4±1.3	NS 0.05 0.003 0.02

ABSTRACT PLUS AB04:
Brugada Syndrome: Novel Insights on Mechanisms

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB04-01

CONDITIONAL KNOCKOUT OF FGF13 IN MURINE HEARTS INCREASES ARRHYTHMIA SUSCEPTIBILITY AND REVEALS NOVEL ION CHANNEL MODULATORY ROLES

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Introduction: Fibroblast growth factor homologous factors (FHFs) bind directly to cardiac voltage gated Na+ channels, and modulate their function. FHF mutations are associated with Brugada syndrome. Although suspected to modulate other ionic currents, such as Ca2+ channels, via acute knockdown experiments in isolated cardiomyocytes, the in vivo consequences of FHF gene ablation on cardiac electrical activity are not known.
Methods: We generated inducible, cardiomyocyte-restricted Fgf13 knockout mice to determine the resultant effects of Fgf13 gene ablation by electrophysiological assay in vivo and in vitro.
Results: Action potentials in Fgf13 knockout mice, compared to Cre control mice, exhibited slower upstrokes, reduced amplitude, and longer durations. Patch clamp recordings from ventricular myocytes isolated from Fgf13 knockout mice demonstrated a ~25% reduction in peak Na+ channel current density and a hyperpolarizing shift in steady-state inactivation. Unexpectedly, in Fgf13 knockout mice the transient outward K+ current (Ito) was reduced by ~36%, but no changes were seen in the sustained outward K+ current or voltage-gated Ca2+ current. Electrocardiograms on Fgf13 knockout mice showed a prolonged QRS duration. Flecainide further prolonged QRS duration and triggered ventricular tachyarrhythmias only in Fgf13 knockout mice, suggesting that arrhythmia vulnerability resulted, at least in part, from a loss of functioning Na+ channels.
Conclusions: FGF13 is a critical cardiac Na+ channel

modulator and Fgf13 knockout mice have increased arrhythmia susceptibility. The unanticipated effect on Ito revealed new FGF13 properties and the unexpected lack of an effect on voltage-gated Ca2+ channels highlight potential compensatory changes in vivo not readily revealed with acute Fgf13 knockdown in cultured cardiomyocytes.

AB04-02

GENOMIC EDITING IN IPSCS ESTABLISHES THAT A RARE TBX5 VARIANT CAUSES BRUGADA SYNDROME

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Introduction: We have identified a novel missense variant in the transcription factor TBX5 (resulting in G145R) in a kindred with Brugada syndrome (BrS) without variants in known BrS genes. Reduced sodium current (INa) due to fewer sodium channels at the cardiomyocyte membrane or mutations impairing channel function is a major cellular mechanism of BrS. TBX5 is known to positively regulate expression of the cardiac sodium channel gene SCN5A. In silico modeling predicts G145R is a loss of function allele, and in preliminary studies we found that TBX5-G145R reduced DNA binding by 97% and TBX5 transcriptional activity in vitro by 61%. These data support but do not prove a causative role for TBX5-G145R in BrS.
Methods: Dermal fibroblasts from TBX5-G145R carriers with BrS and unrelated control donors were reprogrammed to iPSCs. The TBX5 variant was edited to wild-type using CRISPR/Cas9 technology. iPSCs were differentiated to cardiomyocytes (iPSC-CMs) using chemical modification of the Wnt pathway for transcriptional and electrophysiologic studies.
Results: TBX5-G145R (BrS) iPSC-CMs had reduced sodium channel transcript (-73%), membrane-associated protein (-48%), and decreased INa (-97.1±36.5 pA/pF; n=8) versus controls (-211±36.0 pA/pF; n=13, $P<0.05$). After CRISPR/Cas9 editing, sodium channel expression and current density (-198±38 pA/pF; n=10) in iPSC-CMs were restored to control values. Unexpectedly, TBX5-G145R iPSC-CMs also displayed increased late INa (TBX5-G145R: 2.2±0.4%; Control: 0.16±0.05%; n=5, $P<0.05$), increased action potential durations (APDs; TBX5-G145R: 517±72 ms; Control: 321±37 ms; n=7, $P<0.05$), and early and delayed afterdepolarizations (EADs/DADs), all reversed by the late INa blocker ranolazine. These arrhythmogenic properties were also reversed after genomic correction of the TBX5 variant.
Conclusions: These data close the loop between association and causation by proving that TBX5-G145R causes the BrS phenotype of reduced INa and the additional findings of increased late INa, APD prolongation, and EADs/DADs. This approach establishes a new paradigm for studying the pathogenicity of rare variants in congenital arrhythmia syndromes.

AB04-03

EXTENDED GWAS IN BRUGADA SYNDROME UNCOVERS ADDITIONAL RISK ALLELES AT THE SCN5A/SCN10A LOCUS WITH MARKED CUMULATIVE EFFECTS ON RISK FOR THE DISORDER

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Introduction: The Brugada syndrome (BrS) is an inherited cardiac disorder associated with ST-segment elevation in the right precordial leads and a high risk for sudden cardiac death (SCD). The genetic basis of the disorder remains largely unresolved. Rare variants in SCN5A, encoding the major Na-channel isoform in heart, are found in ~20% of cases. We have previously performed a genome-wide association study (GWAS) on 312 patients with BrS and identified 3 common single nucleotide polymorphisms (SNPs) predisposing to the disorder: two at the SCN5A-SCN10A locus and one near the HEY2 gene. Here we aimed to identify additional common SNPs modulating the susceptibility to BrS and/or SCD.
Methods: We have conducted a case-control GWAS in an extended set of BrS patients, totalling 876 BrS probands of North-Western European descent, versus 2,706 ancestry-matched controls.
Results: We confirmed the 3 previously reported association signals at the SCN10A (rs10428132, $p=3.9x10-61$), HEY2 (rs3799708, $p=3.3x10-15$) and SCN5A (rs9833086, $p=3.9x10-12$) loci. Conditional analysis on SNPs at the SCN5A-SCN10A locus revealed 2 additional independent association signals located between the SCN5A and SCN10A genes (rs6422142, $p=1.7x10-11$; rs7638910 $p=4.6x10-12$). No differences in effect size was observed between patients presenting with the BrS ECG at baseline versus after drug challenge. The cumulative effect of the 5 loci on disease susceptibility reached an odds ratio >50 in the presence of ≥ 8 risk alleles versus ≤ 2. Future work will investigate whether additional SNPs can be associated with the BrS phenotype or with arrhythmia by typing additional patients.
Conclusions: The large cumulative effect of the 5 loci (OR>50) reflects the major role of common variants in BrS susceptibility. Our novel findings further reinforce the predominant involvement of the SCN5A-SCN10A locus in the disease and prompt a

reevaluation of the genetic architecture of the BrS for refinement of patient care.
Acknowledgments to GoNL Consortium, KORA Consortium, UK10K Consortium and P. Froguel (The D.E.S.I.R. consortium)

AB04-04

THREE BRUGADA SYNDROME (BRS) ASSOCIATED COMMON VARIANTS PREDISPOSE FOR BRS ECG PATTERN WITHOUT INCREASING THE RISK OF SYNCOPE AND CARDIOVASCULAR DEATH IN THE GENERAL POPULATION OF 6,161 DANISH INDIVIDUALS

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Introduction: A previous genome-wide association study has associated three genetic variants with an increased risk of the rare cardiac arrhythmia disorder Brugada Syndrome (BrS). We sought to investigate the effects of these variants on electrocardiogram (ECG) parameters and the risk of death in a cohort representing the general population.
Methods: A large cohort study of 6,161 Danish individuals, with available electronic ECGs, was genotyped, and subsequently followed for a period of 16 years. The effects on the ECGs were analyzed to correlate ECG parameters with genotype. Furthermore, the risk of syncope, death and ventricular fibrillation and tachycardia were correlated with the number of risk allelles.
Results: Homozygote carriers of the rs6800541 variant located intronic to SCN10A had a 0.05 mm statistically significant elevation of the J-point at the ST-segment (P<0.0001). Homozygote carriers of the rs11708996 variant located intronic to SCN5A had a shortened QTc interval (P = 0.001). The rs6800541 variant also had a borderline significant shortening effect on the QTc interval (P = 0.0523). Both the rs11708996 and rs6800541 variants were shown to have a prolonged effect on the PR interval (P<0.0001 and P<0.0001, respectively) and a prolonged effect on the QRS interval (P = 0.0022 and P<0.0001, respectively). Carriers of the rs9388451 variant located downstream to HEY2 had no statistically significant alterations of their ECGs. None of the variants showed an increased risk on syncope, ventricular fibrillation and tachycardia, and death.
Conclusions: Two out of three BrS associated variants were shown to predispose to BrS ECG pattern in 6,161 Danish individuals, especially with regards to ST-segment elevation. Furthermore, the two variants were shown to shorten the QTc interval and prolong the PR and the QRS interval, suggesting an effect on conduction velocity. None of the variants increased the risk of all-cause mortality.

AB04-05

CORRELATION BETWEEN ST ELEVATION IN TYPE I BRUGADA SYNDROME AND CONDUCTION DELAY IN RIGHT VENTRICULAR OUTFLOW TRACT

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Introduction: The underlying electrophysiological mechanisms that contribute to the (Brugada Syndrome) BrS ECG pattern are still debated. Using non-invasive electrocardiographical imaging (ECGi), we studied whole heart conduction and repolarisation patterns following Ajmaline in BrS individuals.
Methods: 11 concealed Type I BrS and 2 healthy controls (mean age 44±12 yrs; 8 males), underwent an Ajmaline infusion with ECGi vest and ECG recordings. ECGi displays reconstructed electrograms on a patients' CT derived heart geometry, from which epicardial activation maps and activation recovery interval (ARI), an action potential duration surrogate, are derived. ARI and activation timings (AT) across the left and right ventricles (LV/RV) and out flow tract (RVOT) were calculated at baseline and when Type I pattern manifested following Ajmaline (Fig1a). Peak ST elevation (STE) was derived from surface ECG, and correlated to ECGi derived parameters at the same time point.
Results: Following Ajmaline, the RVOT compared to RV or LV, had the greatest increase in conduction delay (AT 5[3-8]ms vs 1[0-4]ms vs 1[0-2]ms; p<0.0001) (Fig1b) and ARI prolongation (68[53-99]ms vs 35[23-46]ms vs 25[9-30]ms; p<0.01). No difference was found in controls. Conduction delay in RVOT, but not RV or LV, correlated to amount of STE (Pearson R 0.8, p<0.001) (Fig1c). No correlation was found between STE and ARI prolongation in the RVOT, RV or LV.
Conclusions: Magnitude of STE in the Type I BrS pattern is attributed to degree of conduction delay in the RVOT and not prolongation in repolarisation time.

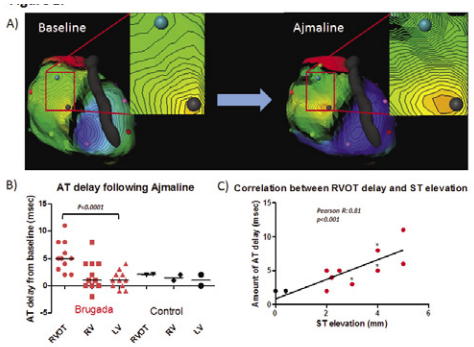

Figure 1a) Isochronal crowding seen over RVOT following ajmaline, and measurement of activation times across region b) Activation time (AT) delay across the different regions. c) Correlation of RVOT conduction delay with ST elevation on ECG. Black denotes control and red denotes Brugada participants

ABSTRACT PLUS AB05:
The Subcutaneous ICD: Improving Efficacy

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB05-01

EVALUATION OF A HIGH PASS FILTER DESIGNED TO REDUCE OVERSENSING IN THE S-ICD

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Introduction: Inappropriate shocks in transvenous ICDs are most often caused by supraventricular tachycardia (SVT), while in the subcutaneous ICD (S-ICD) the most common cause is T-wave oversensing (TWOS). We sought to evaluate the performance of a high-pass filter designed to reduce cardiac oversensing in the S-ICD.
Methods: The algorithm was tested on a dataset of 626 adjudicated episodes (161 TWOS, 328 SVT, 137 VT/VF) from 161 patients. Episodes were evaluated for appropriate decision to treat. TWOS episodes were tested with and without a stored normal sinus rhythm reference ECG. Each episode was run through three devices to account for test system variability, for each device generation (9 evaluations per episode). Repeated measures logistic modeling compared odds of inappropriate decision to treat across generations. TWOS episodes were evaluated at nominal settings of dual zone with rate 200/220. VT/VF and SVT episodes were evaluated at 170/250 for maximal algorithm exposure.
Results: Odds of inappropriate decision for SVT (treated) and VT/VF (untreated) remained unchanged across device generations (table). Inappropriate therapy decision for TWOS (treated) was reduced by 82% compared to the previous generation and 71% compared to generation 1. The time to detect treatable arrhythmias was 8.60 ±3.81 sec in gen 2 and 8.86 ± 3.30 sec in gen 2.5. All episodes of VT/VF undersensed were treated by at least 1 device configuration for each generation.
Conclusions: A new S-ICD algorithm demonstrated significant reduction in shocks for TWOS without a reduction in sensitivity to VT/VF.

		Total Episode Evaluations	Number of Episode Evaluations With Inappropriate Decision			Odds Ratio of Inappropriate Device Decision (95% CI)			
			Gen 1	Gen 2	Gen 2.5	Gen 2.5 vs Gen 1	p-value	Gen 2.5 vs Gen 2	p-value
TWOS	With Reference ECG	483	88	53	16	0.18 (0.08 - 0.4)	<0.001	0.29 (0.13 - 0.67)	0.004
	Without Reference ECG	483	116	76	19	0.17 (0.08 - 0.35)	<0.001	0.24 (0.11 - 0.51)	<0.001
SVT	With Reference ECG	984	29	30	29	1.00 (0.43 - 2.31)	1.0	0.96 (0.42 - 2.22)	0.93
VT/VF	With Reference ECG	411	3	3	3	1.00 (0.13 - 7.91)	1.0	1.00 (0.16 - 6.34)	1.00

AB05-02

PERFORMANCE OF A NOVEL ATRIAL FIBRILLATION DETECTION ALGORITHM FOR USE IN PATIENTS WITH A SUBCUTANEOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATOR

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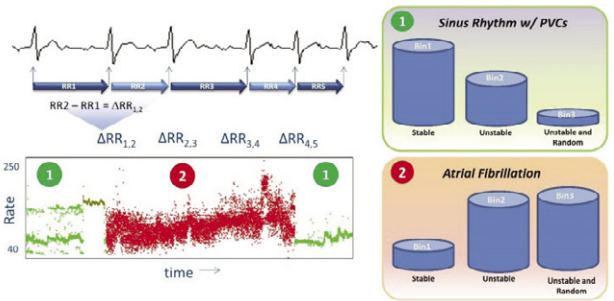
Introduction: The subcutaneous ICD distinguishes between atrial fibrillation (AF) and ventricular arrhythmias; however, an AF diagnostic is currently not available. We evaluated the performance of a novel AF detection algorithm, which could overcome this limitation.
Methods: The algorithm combines ventricular scatter analysis (VSA), a measure of HR variability, with a heart rate (HR) histogram. VSA calculates beat-to-beat RR interval differences, which are categorized into 3 bins: stable, unstable, or unstable and random. In each 192 cycle window, the ratio of beats across the 3 bins differentiates sinus rhythm (SR) from AF. The HR histogram distribution optimizes the algorithm's specificity. The algorithm was developed and separately tested against several publicly available ECG databases.
Results: The validation cohort included 100 patients with and 79 patients without AF. The algorithm correctly excluded AF in all 79 non-AF patients (specificity 100%). Conversely, the AF algorithm correctly identified 94 of the 100 AF patients (sensitivity 94%). AF was not detected when episodes were quite short (<8 minutes; n=4) or associated with a stable ventricular response (n=2).
Conclusions: A novel RR based AF algorithm was developed and tested using publically available ECG databases. The algorithm exhibited very high sensitivity and specificity. If incorporated within existing S ICD systems, it would offer clinicians the ability to monitor for AF without requirement of a transvenous atrial lead.



AB05-03

IMPACT OF GENERATOR LOCATION AND SUB-COIL FAT ON SUBCUTANEOUS-ICD DEFIBRILLATION THRESHOLDS

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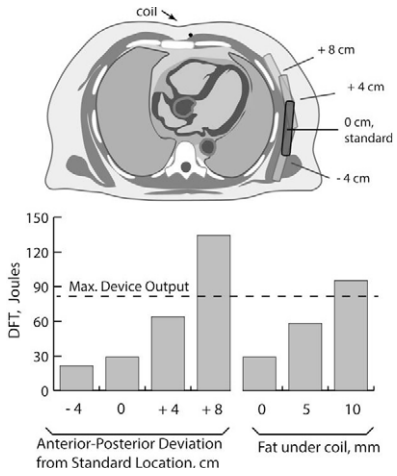
Introduction: Some subcutaneous ICD (S-ICD) patients exhibit unacceptably high defibrillation thresholds (DFT). Implant characteristics associated with high DFTs in S-ICD patients have not previously been described. We sought to determine the impact of S-ICD coil and generator position on DFT based on a computer defibrillation simulation.
Methods: A 3.8 million-element computer model built from MRI images of the thorax was used to simulate the electric fields that occur during defibrillation. Each element represents the electrical properties of the respective tissue or organ. Four generator positions were tested, from posterior to anterior, with 4 cm displacements. The left para-sternal coil was tested with 0, 5, and 10 mm of underlying subcutaneous fat. The DFT for the S-ICD was defined conventionally as the delivered energy required to produce an electric field of 4 Volts/cm in at least 95% of the ventricular myocardium.
Results: DFTs were 22, 29, 64, and 135 Joules for posterior (-4 cm), standard, mid-anterior (+4 cm), and anterior (+8 cm) generator locations. DFTs were 29, 58, and 95 Joules when tested with 0, 5, and 10 mm of fat under the coil. Fat (0-10 mm) under the generator did not substantially impact DFTs.
Conclusions: Our model suggests that an S-ICD implant strategy involving (1) posterior generator location and (2) the coil directly over the ribs without underlying fat is likely to markedly lower DFTs with the S-ICD and reduce the number of patients with unacceptably high DFTs.



AB05-04

IMPACT OF BMI ON SAFETY AND EFFICACY OF THE SUBCUTANEOUS ICD

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Introduction: The subcutaneous ICD (S-ICD) is an established treatment option for patients at high risk for ventricular arrhythmias. Whether efficacy and risk of complications differ by patient (pt) weight remains unknown.
Methods: We analyzed data from the 321 pts enrolled in the S-ICD IDE study. Pts underwent implantation followed by defibrillation testing at 65J. They were categorized into 3 body mass index (BMI) groups: <25 (underweight and normal), 25-30 (overweight) and >30 (obese). Three outcomes were compared across groups: 1) Infection-type complications including erosion, prolonged healing, superficial and system infection; 2) Suboptimal generator/lead position including any revision to a malpositioned device; and 3) Failure of the first 65J shock to defibrillate the first induced VF during implant.
Results: Mean BMI was 29.7 ± 7.3. Seventy-nine pts had BMI <25, 105 pts BMI 25-30 and 137 pts BMI >30. There were no significant differences between BMI groups in rates of infection-type complications (5.1% for BMI <25, 2.9% for BMI 25-30 and 2.9% for BMI >30, p=0.7) or suboptimal generator/lead positioning (3.8%, 3.8% and 5.1%, respectively, p=0.9). Protocol-defined acute conversion success was 100% for 304 evaluable pts. However, the rate of failed first shock at 65J increased across BMI categories (5.2%, 13.3% and 16.5%, respectively, p=0.02 for comparison between BMI>30 vs BMI<25). There were 8 underweight (BMI <18.5) pts, none of whom had infection-type complications or failed first shocks. One had suboptimal device positioning.
Conclusions: While rates of infection-type complications and suboptimal device positioning do not significantly differ according to patient weight, failed 65J shocks may be more common in obese patients.

AB05-05

FIRST REPORT ON COMMUNICATING LEADLESS ANTI-TACHYCARDIA PACEMAKER AND SUBCUTANEOUS IMPLANTABLE DEFIBRILLATOR [[UNSUPPORTED CHARACTER - CODENAME &SHY;]]

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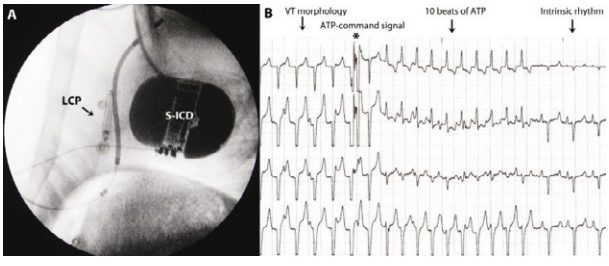
Introduction: With the aim of eliminating lead and pocket related complications, we examine the next step in multi-component leadless cardiac rhythm management (CRM): feasibility of an anti-tachycardia (ATP) leadless cardiac pacemaker (LCP), commanded by an implanted S-ICD through wireless, intra-body, device-device communication.
Methods: The first experiments were conducted in sheep (n=2) with implantation of ATP-enabled LCP and S-ICD prototypes (Boston Scientific). LCP performance, LCP-programmer and LCP-S-ICD communication (both through conductive communication) were tested. ATP-commands, initiated via the S-ICD programmer, were transmitted by the S-ICD to the LCP and LCP response was evaluated.
Results: The LCP and S-ICD were successfully implanted (Panel A). LCP performance was adequate and demonstrated appropriate VVI behavior. Programmer and LCP-S-ICD communication were established without interference. Uni-directional communication between the S-ICD and LCP was successful in all (n=15) attempts (Panel B) resulting in ATP delivery by the LCP (10 beats at 81% of coupling interval). Acute LCP retrieval was successful. Data on additional experiments with automatic S-ICD initiated ATP-delivery in porcine (n=4), canine (n=8) and ovine (n=6) animal models will be added to this analysis.
Conclusions: We present the first proof of concept study with the combined implant of an ATP-enabled LCP and S-ICD. We demonstrated appropriate VVI functionality, successful wireless device-device communication and ATP-delivery by the LCP. Data from 18 animal experiments will be added to this analysis and presented. Further studies on safety and performance are needed.



ABSTRACT AB06:
CIED Implantation Techniques and Outcomes

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB06-01

INCIDENCE OF THORACIC VEIN STENOSIS IN DEVICE UPGRADE PATIENTS: A RETROSPECTIVE ANALYSIS

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Introduction: We sought to identify the rate of thoracic vein occlusion or significant stenosis associated with chronic Cardiac Implantable Electronic Device (CIED) implantation, given the increasing requirement to revise CIED systems to incorporate resynchronisation (CRT) or to address lead problems.
Methods: A radiology database was analysed for the period 2010-2015 at the Princess Alexandra Hospital, Brisbane. Subclavian venography was performed in all CIED patients before revision. Collected data included patient age, CIED type, number and type of implanted leads, duration of lead implantation and side of implant. Stenosis was graded as occluded (100%), severe (50-99%) with presence of collaterals or mild (<50%).
Results: Of the total of 152 patients (age 69±13, 140 left sided CIED), 41 (27%) had stenosis. Of these 9 had occlusion (6%: age 72±10, males = 6), 19 severe stenosis (13%: age 61±14, males=16), and 13 mild stenosis (9%: age 72±9, males = 10). Five patients had a single chamber pacemaker, 17 dual chamber pacemaker, 15 ICD and 4 CRT-D. Mean interval from implant was 7.0±3.8 years. Collateralisation was identified in 15 (10%) patients and was associated with higher grade stenosis. Risk of stenosis was not increased by lead type or number (1.8±0.5 leads without stenosis vs 2.0±0.7 leads with stenosis) and no stenosis were identified in any of the 12 patients with right sided CIEDs.
Conclusions: At a mean of 7 years from CIED implant, stenosis of the thoracic venous system occurred in 27% of cases, of which two thirds were total or severe. The risk of stenosis was not associated with either the type or number of leads. Given the frequency of CIED-associated venous stenosis, subclavian venography should be performed prior to lead revision or device upgrade.

AB06-02

RIGHT VENTRICULAR SEPTAL PACING IS ASSOCIATED WITH HIGHER RATES OF ATRIAL FIBRILLATION

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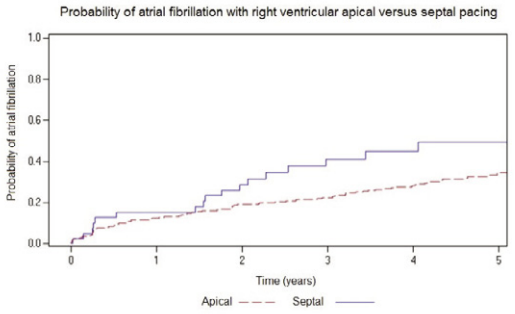
Introduction: Right ventricular (RV) pacing appears to have detrimental effects on cardiac function and outcomes. The RV septum has been proposed as a more physiologic pacing location than the typical apical position. Results from prior studies have been heterogeneous and limited by short follow-up. This study aimed to compare long-term outcomes between patients with high levels of apical versus septal pacing.
Methods: All patients who underwent dual-chamber pacemaker placement from 2004-2013 and were ventricular paced more than 40% of the time were included. Lead position was assessed by chest radiograph. Demographic and echocardiographic data were taken from the medical record. Outcome rates at 5 years were compared using Kaplan-Meier analysis.
Results: During the study period, 1187 patients with dual-chamber pacing were eligible for study based on their RV pacing percentages. Apical and septal leads were present in 1089 and 98 patients respectively. Kaplan-Meier analysis demonstrated a significantly higher rate of new onset atrial fibrillation with RV septal pacing compared to apical pacing at 5 years (Figure). There were no significant differences observed in the incidence of subsequent heart failure, ICD/CRT upgrade, mitral or tricuspid regurgitation, or left ventricular ejection fraction. There was a trend toward lower mortality in the septal group, but this did not meet statistical significance (p = 0.06).
Conclusions: RV septal lead position was found to be associated with a higher rate of atrial fibrillation than the traditional apical lead position. It is foreseeable that the development of this arrhythmia limits the beneficial effects of septal pacing.



AB06-03

TWELVE LEAD ECG AND STANDARD FLUOROSCOPY AT PACEMAKER IMPLANT DOES NOT RELIABLY PREDICT RIGHT VENTRICULAR SEPTAL PACING LEAD POSITION COMPARED WITH HIGH RESOLUTION CT SCANNING

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Introduction: Traditionally standard fluoroscopy (anteroposterior (AP) and 30° left anterior oblique (LAO)) and 12 lead ECG can be used to assess right ventricular (RV) apical (RVA) and septal (RVS) lead position during pacemaker implant. We performed a comparison between post procedure high resolution contrast cardiac CT imaging and a 12 lead surface ECG in patients with permanent pacemakers.
Methods: Eighteen patients with dual chamber pacemakers, 10 RVS and 8 RVA placed fluoroscopically using AP and LAO 30° views at implant, underwent high resolution contrast cardiac CT imaging and ECG. On cardiac CT the RV was partitioned arbitrarily into three long-axis segments (right ventricular outflow tract, middle and apex), and two short-axis segments (septal and non-septal). A true septal lead position was defined if the pacing lead tip pointed towards the left anterior descending artery (LAD) and if late contrast filling outlined the RV cavity enhancing identification of the septum.
Results: Lead tip position was identified in all patients. On CT imaging, of leads placed in RVS position, 7 were on the anterior RV wall, 2 were at the anteroseptal junction, and 1 was lower septum. The ECGs consistently showed a QRS axis of -90°, an absent R wave in V1 and a positive R wave in V6 in all cases. For the 8 RVA leads, 4 were anterior, 2 septal, 2 anteroseptal.

The ECG axis varied between -90 and +110°, an absent R wave in V1 in all cases but a positive R wave in V6 in 4. The QRS duration for RVNA was 157+24ms compared with 170+13ms for RVA pacing.
Conclusions: CT provides a clear image of the pacing lead tip position. Although the ECG differentiated RVA from RVS lead position it does not allow accurate lead tip position compared to CT.

AB06-04

SUBCUTANEOUS IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR IMPLANTATION ON UNINTERRUPTED ANTICOAGULATION

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Introduction: The safety of implantation of transvenous pacemakers and implantable cardioverter-defibrillators (ICDs) with uninterrupted therapeutic warfarin therapy has been established. Very limited data are available on the safety of subcutaneous ICD (S-ICD) implantation on warfarin and antiplatelet therapies.
Methods: We evaluated procedural and post-procedural outcomes in patients undergoing S-ICD implantation from February 2011 to November 2015 at our academic center.
Results: One hundred one S-ICDs were implanted at our academic center of which 64 were male. The mean age was 53 years +/-13.9 years. Fifty-five (54.5%) were implanted for primary prevention and 61 (60.4%) were implanted using a three incision technique. Eighteen patients (17.8%) were actively taking warfarin and had an INR of at least 1.60 on the day of the procedure with a mean INR of 2.13 +/-0.51 and range 1.60-3.30. Seven patients were on dual antiplatelet therapy in addition to warfarin, 17 patients were on dual antiplatelet therapy alone, and 29 patients (27.7%) were not taking either. One patient on warfarin had a pocket infection compared to three patients not on warfarin (p value = 0.7). Of the three pocket infections in patients not on warfarin, two required device explant. There were no intra- or postoperative bleeding complications in any patients regardless of warfarin or antiplatelet therapy. Procedure time in patients taking warfarin was 59.9 minutes +/-14.5 minutes and 59.6 minutes +/- 14.9 minutes in patients not on warfarin.
Conclusions: Patients implanted with S-ICDs on uninterrupted warfarin show no increase in bleeding complications or in post-operative device infections.

AB06-05

DISLODGMENT RATES OF IMPLANTED DF4 ICD LEADS INCREASE IN THE PRESENCE OF ATRIAL AND CORONARY SINUS LEADS

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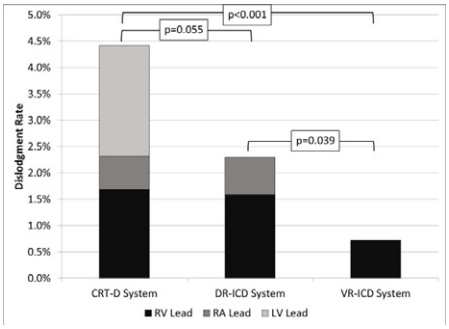
Introduction: It is known that ICD pulse generator replacement complications increase in proportion to replacement procedure complexity. However, there are no reliable data on complication rates at implantation of DF4 ICD leads. We hypothesized that complication rates may increase with the number of implanted leads.
Methods: We analyzed data from an FDA mandated longitudinal surveillance study of DF4 ICD leads. Data from implantation of 1717 DF4 leads were collected from 111 investigational sites. We report data up to 6 months of follow-up. Dislodgment rates were stratified by whether the DF4 lead was implanted in a single lead system (VR), with an atrial lead (DR), or with atrial and coronary sinus leads (CRT-D). Adverse events were collected starting at implantation, including prior to pocket closure.
Results: There were 548 VR, 694 DR, and 475 CRT-D systems implanted. Of 41 total lead dislodgments, 23 (1.3% of RV leads) were DF-4 leads. The DF4 lead dislodgment rate trended higher in complex (DR or CRT-D) compared to simple (VR) systems (p=0.18). DF4 dislodgment rates were highest for CRT-D (1.68%) and DR (1.59%), and lowest for VR systems (0.73%). Total dislodgment rate differences were significant (CRT-D v. VR, p<0.001; DR v. VR, p=0.039). Most RV lead dislodgments (91.3%) occurred within 30 days.
Conclusions: Six month lead dislodgment rates for DF4 leads increase with implantation of a right atrial lead. Adding a coronary sinus lead (CRT-D) does not increase RV lead dislodgement beyond that seen in DR systems. This effect may be related to lead-to-lead binding, increased manipulation to place additional leads, or variations in myocardial substrate.



AB06-06

LONG-TERM IMPACT OF THE RIGHT VENTRICULAR STIMULATION SITE ON LEFT VENTRICULAR SYSTOLIC FUNCTION AND MORTALITY IN PACEMAKER RECIPIENTS WITH PRESERVED EJECTION FRACTION

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Introduction: Right ventricular (RV) pacing may lead to asynchronous contraction, left ventricular (LV) systolic dysfunction, and heart failure. RV-apical pacing changes the physiological electrical activation pattern of the ventricles more than a septal lead position and might therefore be potentially more harmful on LV systolic function. The role of the stimulation site (apical vs. septal) in patients (PTS) treated with pacemakers (PM) for atrioventricular block (AVB) is still uncertain.
Methods: Echocardiographic evaluation (ECHO) of PTS with AVB and normal LV function (LVEF > 55%) at the time of PM implantation and after a follow-up (FU) of >2 months. PTS with primary CRT- or ICD-indications were excluded. Main outcome measures were deterioration of LV systolic function (LVEF < 41%) or death from any cause. All results were compared between apically paced vs. septally paced PTS (apicPTS vs. septPTS).

Results: Evaluation of 1759 PTS treated with a PM for standard antibradycardic indication at our institution between 2005-2009. Of those 538 PTS with AVB (53% male, mean age 74yrs) met the entry criteria and were followed for 3.6±1.8yrs. In 141 (26%) PTS the implanted RV electrode was positioned in the RV apex (group apicPTS), in 397 (74%) PTS a septal localization was chosen (group septPTS). Baseline patient characteristics (age, sex, underlying diseases) were not significantly different between the two groups. A normal LV function at the time of implant was present in 386 (72%) PTS, (apicPTS: n=105, (74%) vs. septPTS: n=281, (71%), n.s.). Of those, at the end of FU, LV function was preserved in 316 (82%) PTS (apicPTS: n=91, (87%) vs. septPTS: n=225 (80%), p=0.3). A total of 22 (5%) PTS (apicPTS: n=5, (5%) vs. septPTS: n=17, (6%), p=0.4) with initially normal LV function (EF >55%) experienced deterioration of LV systolic function (EF<41%). At the end of FU 54 (14%) PTS had died. There was no significant difference in mortality between both groups (apicPTS: n=19, (18%) vs. septPTS: n=35, (12%), p=0.3).
Conclusions: In PTS with AVB and permanent RV pacing the development of severe LV dysfunction is infrequent when there is a normal systolic LV function at the time of PM insertion. LV deterioration or mortality do not seem to be influenced by RV lead position.

ABSTRACT PLUS AB07: Biomonitors for Arrhythmia Detection

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB07-01

REAL WORLD COMPARISON OF IN-HOSPITAL REVEAL LINQ INSERTION INSIDE AND OUTSIDE OF THE CARDIAC CATHETERIZATION OR ELECTROPHYSIOLOGY LABORATORY

Sean C. Beinart, MD, FHRS, Andrea Natale, MD, FHRS, Atul Verma, MD, FRCP, Alpesh N. Amin, MD, Scott Kasner, MD, MSc, Hans-Cristoph Diener, MD, PhD, Maurizio Del Greco, MD, Bruce L. Wilkoff, MD and Suneet Mittal, MD. Washington Adventist Hospital, Takoma Park, MD, Texas Cardiac Arrhythmia Institute, St. David's Medical Center, Austin, TX, Southlake Regional Health Centre, Newmarket, ON, Canada, University of California, Irvine, CA, University of Pennsylvania, Philadelphia, PA, University Hospital Essen, Essen, Germany, Hospital of Rovereto, Trento, Italy, Cleveland Clinic, Cleveland, OH, The Valley Hospital, Ridgewood, NJ

Introduction: The Reveal LINQ™ is a miniaturized insertable cardiac monitor (ICM) involving a minimally invasive procedure. Limited feasibility and safety data are available regarding insertion procedures within the hospital but outside of the cardiac catheterization (CATH)/electrophysiology (EP) laboratory. This is a status update of the Medtronic Reveal LINQ™ Registry.
Methods: Ongoing, prospective, observational multi-center study evaluating real-world performance of the ICM. A total of 1200 patients will be enrolled and followed prospectively from insertion through 3 years. All categorical values were compared using the Fisher's Exact test.
Results: Patients (54% male, age 62.1±16.2 years) were enrolled at 14 centers in the US and 5 in Europe. ICM insertions were all performed either in-lab (CATH, EP lab, or operating room) (n=221) or out-of-lab (clean/procedure room or lab holding area) (n=160). Baseline characteristics were similar in both groups except for age, gender, history of COPD or cancer. No significant differences in infection or serious adverse events (SAE) were detected. The out-of-lab group had 2 (1.3%) infections (resolved with oral antibiotics) and 1 (0.6%) patient had a SAE (erosion). The in-lab group had 1 (0.5%) infection also considered a SAE (resulting in explant). There were significant differences in procedure characteristics.
Conclusions: This real-world comparison shows significant differences with respect to how the procedure is performed in-lab vs. out-of-lab with no apparent effect on infection or SAE.

Procedure Characteristics	In-lab n=221	Out-of-lab n=160	P-value
Pre-procedural antibiotics	85 (38.5%)	7 (4.4%)	<0.0001
% IV	85 (38.5%)	1 (0.6%)	<0.0001
Post-procedural antibiotics	29 (13.1%)	2 (1.3%)	<0.0001
% IV	21 (9.5%)	1 (0.6%)	<0.0001
Device fixation with sutures	11 (5.2%)	1 (0.6%)	0.0153
Wound closure method: suture	73 (33.0%)	8 (5.0%)	<0.0001
Wound closure method: staples	9 (4.1%)	103 (64.4%)	<0.0001
Wound closure method: surgical glue	56 (25.3%)	19 (11.9%)	0.0011
Wound closure method: steri strips	141 (63.8%)	141 (88.1%)	<0.0001

AB07-02

PREDICTING ATRIAL FIBRILLATION OR FLUTTER (PREDATE-AF) STUDY: INTERIM ANALYSIS

Javed M. Nasir, MD, Adam Marler, MD, William Pomeroy, MD, Matthew C. Hann, MD, Tina Baykaner, MD, MPH, Richard Stoll, RN, Katie Hursey, BSN, Angela Meadows, MSN, NP, RN, Jennifer Walker Weber, MSN, NP, RN and Steve Kindsvater, MD. Stanford University, Stanford, CA, Keesler Medical Center, Biloxi, MS

Introduction: The incidence of atrial fibrillation (AF) and atrial flutter (AFl) depends upon the population studied and intensity of monitoring with many of the risk factors for development of AF/AFl being the risk factors predictive of thromboembolic complications. The incidence of AF in an asymptomatic population at high risk of AF using an insertable cardiac monitor (ICM) is not known.
Methods: Investigator initiated, prospective, single center trial with planned enrollment of 350 asymptomatic subjects with no history of AF/AFl and CHADS2-VASc score ≥2 to screening for AF/AFl with an ICM. Subjects will be followed for 18 months to assess for incidence of AF/AFl ≥6 min. Enrollment was started 6/2013 and was closed 12/2014 at investigators' discretion due to slowing enrollment. Here we report an interim analysis with all subjects having >12 months follow-up and planned trial completion 6/2015.
Results: 249 subjects were enrolled (4 withdrew consent or were lost to follow-up). The mean age was 73±7.1 and CHADS2-VASc score was 4.5±1.5. The Kaplan-Meier survival curves are below. With a mean follow-up of 444±181 days the incidence of AF/AFl was 22% (53/245 AF, 1/245 AFl). The mean time to detection was 136.4±135.8 days with 15/54 having AF/AFl detected in the first 30 days. There was no significant difference in AF free survival when subjects with CHADS2-VASc score ≥5 were compared to a score of ≤4 (p=0.46, log-rank), or when subjects with a history of remote stroke/TIA were compared to subjects without such history (p=0.41, log-rank).
Conclusions: In this large, prospective, cohort of patients with no history of AF/AFl and a CHADS2-VASc score ≥2, 22% developed > 6 minutes of AF/AFl at interim analysis.

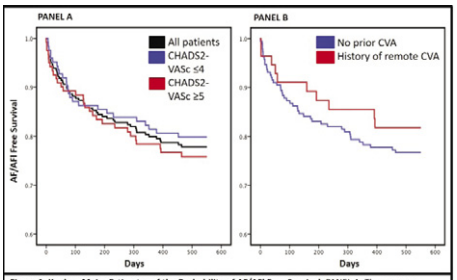

Figure 1. Kaplan–Meier Estimates of the Probability of AF/AFl Free Survival: PANEL A: There was no significant difference in AF free survival between patients with a CHADS2-VASc ≥5 and patients with a score of ≤4 (nominal P=0.460 by the log-rank test). PANEL B: There was no significant difference in AF free survival between patients with and without a history of remote CVA (nominal P=0.411 by the log-rank test)

AB07-03

USE OF A PATCH WORN WIRELESS MULTI-SENSOR BIOMETRIC MONITOR FOR HOSPITALIZED PATIENTS NOT REFERRED TO A TELEMETRY UNIT

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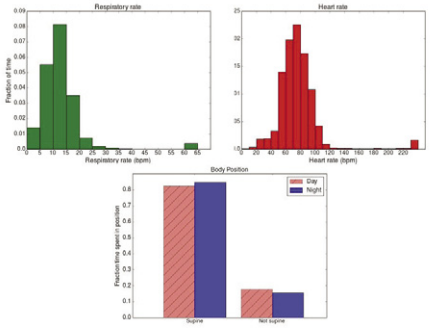
Introduction: New wireless body worn sensors can provide accurate cardiac rhythm monitoring, have additional sensing capability, a favorable form factor and don't require any additional hospital infrastructure.
Methods: We offered 33 patients (mean age 57.8±19.2 years, 31% male) admitted to a general medical ward at USC Keck Hospital access to a patch-based wireless sensor that was worn for their admission (mean 2.2±1.1 days) that measured continuous ECG, respiratory rate, body position and motion (Zephyr LIFE, Medtronic, Inc). Data on all measures was retrospectively reviewed after discharge and ECG tracings adjudicated for arrhythmias. Admission diagnoses included arenal failure, pancreatitis, cholecystitis, GI bleed, neutropenia, bacteremia and pneumonia.
Results: All patients tolerated the sensor on their torso and there were no adverse events associated with monitoring. The mean heart and respiratory rates were 76±30 bpm and 13±9 breaths/min, respectively. Patients were in a supine versus upright position for 83 % of the monitoring period and only 3 of 33 subjects (9%) were upright for at least 50% of their hospital stay. Most subjects did not increase their activity over the course of their stay. Actionable arrhythmias were detected in 4 subjects with no prior history.
Conclusions: Patients admitted to a general medical ward, with diverse diagnoses, who were not referred to telemetry can be monitored for multiple biometric and activity measures throughout their stay. Most patients are supine for the majority of their stay and this is a potential target for intervention.



AB07-04

FEASIBILITY OF AUTOMATED DETECTION OF SLEEP APNEA USING IMPLANTABLE PACEMAKERS AND DEFIBRILLATORS

Giovanni B. Forleo, MD, PhD, Luca Santini, MD, PhD, Sergio Valsecchi, PhD, Domenico G. Della Rocca, MD, Mariolina Lovecchio, BA, Andrea Natale, MD, FHRS and Luigi Di Biase, MD, PHD, FHRS. Policlinico Tor Vergata, Rome, Italy, Boston Scientific, Milan, Italy, University of Rome Tor Vergata, Rome, Italy, Texas Cardiac Arrhythmia Institute, Austin, TX, Texas Cardiac Arrhythmia Institute at St. David's Medical Center and Albert Einstein College of Medicine at Montefiore Hospital, Austin, TX

Introduction: Breathing disorders are common but still underdiagnosed in patients with cardiovascular disease. Sleep apnea is associated with increased cardiovascular risk, especially in patients with heart failure, thus diagnosing and possibly treating apnea is an issue in the management of the disease. Some pacemakers (PM) and implantable cardioverter-defibrillators (ICD) are now able to monitor intrathoracic impedance for automatic detection of sleep apnea events. The aim of the study was to evaluate the performance of the Respiratory Disturbance Index (RDI) calculated by the ApneaScan algorithm (Boston Scientific).
Methods: Patients underwent overnight polysomnography and the apnea-hypopnea index (AHI) was computed as the number of apneas and hypopneas divided by analyzed time minus movement time and standing position time. The PM/ICD-derived RDI value was simultaneously recorded and compared to the AHI, considered as gold-standard measurement.
Results: Twenty-eight patients (aged 71±8 years, 18 males) were studied. Seventeen patients received an ICD and the remaining patients a PM. The mean AHI value during the study night was 21±17 episodes/h while the mean RDI was 33±22 episodes/h. RDI values correlated with AHI ($r=0.81$, $p<0.001$). The Bland-Altman agreement analysis of AHI-RDI revealed a bias between measurements of -12 episodes/h [limits of agreement: -38 to 14 episodes/h]. Severe apnea (AHI≥30) was diagnosed in 14 patients. An optimal RDI cut-off of 47 episodes/h enabled detection of severe apnea with 100% sensitivity and specificity.
Conclusions: The agreement between AHI and RDI measurements automatically recorded during the sleep study night was good. Moreover, the screening performance of APNEA Scan algorithm seemed high in identifying patients with severe disordered breathing, thus requiring further investigations on apnea severity and form, and possibly necessitating additional therapy.

AB07-05

A DUAL SENSING SCHEME TO REDUCE INAPPROPRIATE DETECTION OF BRADYCARDIA AND PAUSES IN AN INSERTABLE CARDIAC MONITOR

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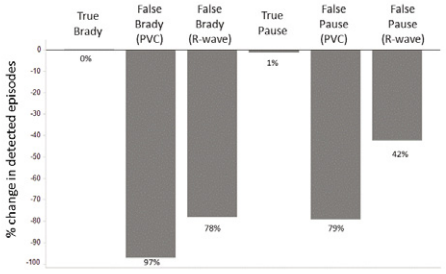
Introduction: Under sensing of premature ventricular beats (PVC) and low amplitude R-waves were identified as primary causes for inappropriate bradycardia and pause detection in insertable cardiac monitors (ICM). We developed an algorithm based on dual sense channels to reduce these inappropriate episodes.
Methods: Pts with large numbers of detected bradycardia and pause episodes were considered in the data cohort with only one episode (the most recent) per pt being considered to avoid bias

of multiple episodes per pt. The primary sense channel uses an auto adjusting sensitivity threshold to allow for proper sensing of the R-wave and avoid T-wave over sensing. In the enhanced algorithm, a second sensing threshold is used with a long blanking (520 ms) and fixed lower sensitivity threshold looking for evidence of under sensed signals. %change in true and false bradycardia and pause detection with the enhanced algorithm is reported.
Results: The dataset consisted of 388 bradycardia episodes (269 true episodes, 101 false episodes due to PVCs, and 18 false episodes due to reduced r-wave amplitudes) and 388 pause episodes (189 true episodes, 57 false episodes due to PVCs, and 160 false episodes due to reduced r-wave amplitudes). The enhanced algorithm reduced inappropriate bradycardia and pause episodes caused by under sensing by 94% and 52% respectively with minimal to no reduction in true episodes (figure).
Conclusions: An enhanced algorithm for bradycardia and pause detection in ICMs incorporating a dual sense scheme can substantially reduce inappropriate detection with minimal reduction in appropriate detection. This algorithm needs further validation using a larger independent dataset.



ABSTRACT AB08:
Novelties in CRT and Defibrillations

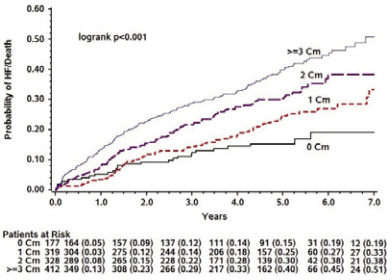
Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB08-01

MULTIPLE COMORBIDITIES AND RESPONSE TO CRT-D: RESULTS FROM THE MADIT-CRT LONG-TERM FOLLOW-UP STUDY

Emily P. Zeitler, MD. Duke University Hospital, Durham, NC

Introduction: Data on cardiac resynchronization therapy with defibrillator (CRT-D) in heart failure (HF) patients with multiple comorbidities are limited. We sought to determine whether the benefits of CRT-D in MADIT-CRT are associated with comorbidity burden.
Methods: We examined 1236 MADIT-CRT patients (500 ICD, 736 CRT-D) with LBBB and 0, 1, 2, or ≥3 comorbidities including: renal dysfunction, hypertension, diabetes, coronary artery disease, history of atrial arrhythmias, history of ventricular arrhythmias, and cerebrovascular accident. We examined percent change in LV end diastolic volume (LVEDV), LV end systolic volume (LVESV), and LVEF at 1-year in CRT-D patients by comorbidity group. We then analyzed risk of HF events or death in CRT-D vs. ICD patients by comorbidity group.
Results: In CRT-D patients, LVEDV, LVESV, and LVEF changes differed by comorbidity group ($p<0.05$ for all) with the greatest improvements in those with 0 comorbidities. In an age-adjusted model, there was increasing HF/death risk by increasing comorbidities (HR 1.37, $p<0.001$), and patients with 2 or ≥3 had increased HF/death risk compared with those with 0 comorbidities ($p<0.01$ for both). During the median 5.6 years of follow-up however, there was no interaction between comorbidity burden and HF/death benefit of CRT-D (0 comorbidity: HR 0.65, 1: HR 0.49, 2: HR 0.40, or ≥3: HR 0.53, interaction p = 0.958).
Conclusions: Among MADIT-CRT CRT-D patients with LBBB, increased comorbidity burden was associated with less reverse remodeling. During long-term follow-up, despite differences in HF/death risk among groups, the burden of comorbidity does not appear to compromise the benefits of CRT-D compared with ICD alone.



AB08-02

IMPACT OF BASELINE PR INTERVAL ON OUTCOMES AFTER CRT IN PATIENTS WITH NARROW QRS COMPLEXES AND ECHOCARDIOGRAPHICALLY DETECTED DYSSYNCHRONY: A SUBGROUP ANALYSIS OF THE ECHO-CRT TRIAL

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Introduction: Cardiac resynchronization therapy (CRT) is now known not to be beneficial for patients (pts) with narrow QRS complexes. We assessed the impact of baseline PR interval on CRT outcomes [death and/or heart failure (HF) hospitalization] in the ECHO-CRT study. Briefly, ECHO-CRT randomized HF pts with QRS duration<130 ms and echo-detected dyssynchrony to CRT-ON or CRT-OFF.
Methods: The entire ECHO-CRT cohort was divided into 2 groups, based on baseline PR interval: PR≤160 ms, and PR>160 ms. Hazard ratios were calculated separately for the 2 groups.
Results: In the CRT-ON subset, there were 109 pts with PR≤160 ms and 291 pts with PR>160 ms; there were no significant baseline differences, except a slightly narrower QRS in pts with PR≤160 ms (102.2±12.2 vs 106.6±16.3 ms, P=0.011). The primary endpoint of Death or HF hospitalization, and the individual secondary endpoints of Death alone and HF hospitalization alone, were all significantly reduced only in the PR≤160 group compared to the PR>160 group. These differences were not seen in the CRT-OFF subset. See Table.
Conclusions: Although there was no benefit from CRT in all HF pts with narrow QRS and echo-detected dyssynchrony in the ECHO-CRT study, pts with baseline PR≤160 ms derived statistically significant benefits in the prespecified primary and secondary endpoints. This may be related to less preexisting conduction system disease, as evidenced by shorter baseline

QRS durations. This data may explain why individual pts showed improved clinical status, despite over all negative trial results.

CRT Status	CRT Off			CRT On		
	PR≤160 ms (n=112)	PR>160 ms (n=290	Hazard Ratio P value	PR≤160 ms (n=109	PR>160 ms (n=291)	Hazard Ratio P value
Death or HF Hospitalization	26 (23.2%)	75 (25.9%)	HR=1.14 (0.73-1.78), P=0.567	17 (15.6%)	99 (34.0%)	HR=2.47 (1.48-4.14), P<0.001
Death alone	4 (3.6%)	21 (7.2%)	HR=2.17 (0.74-6.32), P=0.156	6 (5.5%)	39 (13.4%)	HR=2.64 (1.12-6.24), P=0.027
HF Hospitalization alone	23 (20.5%)	67 (23.1%)	HR=1.14 (0.71-1.84), P=0.579	16 (5.5%)	83 (28.5%)	HR=2.17 (1.27-3.71), P=0.004
Cardiovascular Death	1 (0.9%)	15 (5.17%)	HR=6.08 (0.80-46.05), P=0.081	6 (5.5%)	31 (10.7%)	HR=2.11 (0.88-5.06), P=0.094
Total Hospitalizations for Worsening HF	44	137	RR=1.13 (0.61-2.08), P=0.7	32	197	RR=2.39 (1.29-4.45), P=0.006

AB08-03

CARDIAC RESYNCHRONIZATION THERAPY IN THE ELDERLY WITH OR WITHOUT AN IMPLANTABLE DEFIBRILLATOR

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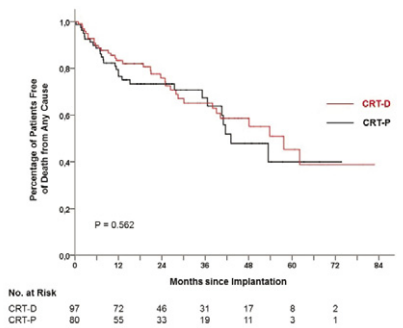
Introduction: Cardiac resynchronization therapy (CRT) is an effective treatment option in elderly patients, but the additional benefit of a defibrillator (ICD) in these patients is not evidenced.
Methods: Patients at the age of ≥ 75 years who underwent implantation of either a CRT-pacemaker (CRT-P) or CRT-defibrillator (CRT-D) were identified out of hospital records. Only patients with an established indication for CRT and a primary prevention ICD were included in the analysis. Patient characteristics, procedural and follow-up data and all-cause mortality were compared between the two groups.
Results: Between January 2008 and August 2014 two-hundred forty-five seniors were implanted with a CRT device in our department, whereof 80 patients with CRT-P and 97 patients with CRT-D represent the two study groups. Patients in the CRT-P group were more often females (44 vs. 25%; p<0.001), older (82.6 ± 4.5 vs. 77.8 ± 1.9 years, p<0.001), had a better LV-EF (29.5 ± 5.7 vs. 27.4 ± 6.0 %; p=0.019) and narrower QRS-complexes (150 ± 19 vs. 158 ± 18ms; p=0.025). During a mean follow-up of 25.7 ± 18.9 months 62 (35%) of the 177 study patients died, 28 (35%) in the CRT-P and 34 (35.1%) in the CRT-D group, respectively. The Kaplan-Meier analysis of survival probability showed no significant difference (p= 0.562) between the two groups. Inappropriate ICD interventions were recorded in 4 patients (4.1%) and 5 patients (5.2%) received appropriate therapies in the CRT-D group.
Conclusions: An additional ICD has no impact on survival in elderly patients implanted with a CRT device. A randomized controlled trial has to prove this finding.

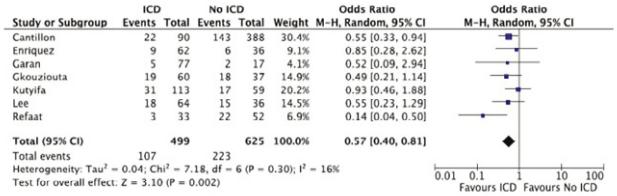


AB08-04

ICDS ARE ASSOCIATED WITH GREATER SURVIVAL AFTER LVAD IMPLANTATION: A META-ANALYSIS

Mohammed Shurrab, MD, MSc, Stephen Pettit, MD, Soon J. Park, MD, Safaa Atturman, MD, Aesha Sbaih, MD, Ghaith Khaleel, MD, Eugene Crystal, MD, Mark Petrie, MD and Saleem Haj-Yahia, MD. An-Najah National University Hospital, An-Najah National University, Nablus, Palestinian Territory, Papworth Hospital NHS Foundation Trust, Cambridge, United Kingdom, University Hospitals Case Medical Center, Cleveland, OH, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada, Golden Jubilee Hospital, Glasgow, United Kingdom

Introduction: Ventricular arrhythmias (VA) are common in patients with left ventricular assist devices (LVAD) but may be well tolerated. The role of implantable cardioverter defibrillators (ICD) in LVAD-supported patients is controversial. The aim of this meta-analysis is to explore the association between ICDs and survival in LVAD patients.
Methods: An electronic search was conducted. We included studies that reported outcomes in LVAD patients stratified by the presence or absence of an ICD. The primary outcome was all cause mortality. Odds ratios (OR) were reported for dichotomous variables.
Results: Seven studies (6 retrospective and 1 prospective non-randomized) including 1124 adult patients were identified. An ICD was present in 499 LVAD patients. Baseline characteristics were similar between LVAD with ICD versus LVAD only groups (age: 56±4 vs. 53±5 years, p= 0.3; male gender: 86% vs. 78%, p= 0.6; ischemic heart disease: 42% vs. 59%, p=0.5 and left ventricular ejection fraction: 17±2% vs. 15±3%, p=0.5). Observed all cause mortality was lower in the LVAD with ICD group, compared with the LVAD only group (21% vs. 36%, OR 0.57 (95% confidence interval [CI] 0.40; 0.81), p=0.002). No significant heterogeneity was noted for the comparison (I2=16%, P=0.30). The rate of inappropriate therapies among ICD patients was 10% out of all delivered therapies.
Conclusions: Concomitant use of ICDs is associated with greater survival in observational studies of LVAD patients. This association may be due to confounding or represent a protective effect of ICD therapy in LVAD patients. A randomized controlled trial is required to define the role of ICDs in LVAD patients.



AB08-05

IMPLANTABLE CARDIOVERTER DEFIBRILLATOR THERAPY IN PATIENTS WITH IMPROVED LEFT VENTRICULAR EJECTION FRACTION A META ANALYSIS

Aiman M. Smer, MBChB, Mohsin Salih, MBChB, Alok Saurav, MD, Mohamed Ayan, MD, Muhammad Soubhi Azzouz, MD, Ahmed Abuzaid, MD, Arun Kanmanthareddy, MD, Saurabh Aggarwal, MD and Hussam Abuissa, MD. Creighton University Medical Center, Omaha, NE, St Luke's Hospital, Chesterfield, MO, The University of Kansas Medical Center, Kansas City, KS, Chicago Medical School, North Chicago, IL, Creighton University, Omaha, NE

Introduction: There are limited data on the long term risk of malignant arrhythmias and the need for Implantable cardioverter defibrillator (ICD) therapy in patients with improved left ventricular ejection fraction (LVEF) who no longer meet criteria for primary prevention. We performed this meta-analysis to evaluate the effect of LVEF improvement on the incidence of appropriate ICD therapy.
Methods: We searched PubMed, Cochrane library and Embase databases for English language studies evaluating the effect of LVEF improvement on ICD therapy during follow-up. We used search terms “Implantable Cardioverter Defibrillator” and “Ejection Fraction”. Odd ratio (OR) and 95% confidence intervals (CI) computed using the Der Simonian and Laird random effect model. Sensitivity and cumulative analysis was performed for each outcome.
Results: We identified a total of 10 studies with 2651 patients included in our analysis. LVEF improvement was defined as LVEF of > 35% during follow up. LVEF improvement was noted in 1180 patients of whom 81(6.8%) patients received appropriate ICD therapies. In the group without LVEF improvement, 16.9% of the patients received appropriate ICD therapies. The odds of receiving ICD therapy is low (OR 0.42; 95% CI 0.25-0.70, P = 0.00, I2=55.49) in the group with LVEF improvement who no longer met the criteria for primary prevention of ICD implantation at the time of generator replacement. The number needed for appropriate ICD therapy in the group with LVEF improvement is 10. Compared with the group without LVEF improvement, the mortality rate is less in the group with LVEF improvement (OR 0.45; 95% CI 0.28-0.70, P = 0.00, I2=35.22). No evidence of publication bias was found.
Conclusions: The results of our study show that improvement in LVEF significantly decreases the risk of ICD therapies and is associated with lower mortality. However, improvement in LVEF doesn’t totally eliminate the risk of arrhythmic events.

AB08-06

STUDY OF THE WEARABLE CARDIOVERTER DEFIBRILLATOR IN ADVANCED HEART-FAILURE PATIENTS (SWIFT)

Alon Barsheshet, MD, Valentina Kutyifa, MD, Theodora Vamvouris, MS, Arthur J. Moss, MD, Yitschak Biton, MD, Leway Chen, MD, Eugene Storozynsky, MD, Chingping Wan, MD, Steven J. Szymkiewicz, MD and Ilan Goldenberg, MD. Rabin Medical Center, Petah Tikva, Israel, University of Rochester Medical Center, Rochester, NY, ZOLL, Pittsburgh, PA, Lifecor Inc., Pittsburgh, PA, University of Rochester Medical Center - Heart Research Follow-up Program, Rochester, NY

Introduction: Patients hospitalized with decompensated heart failure (HF) have high morbidity and mortality during the early post-discharge period. The wearable cardioverter defibrillator (WCD) may allow stabilization until reassessment for an implantable cardioverter defibrillator (ICD) among high-risk HF patients. However, there is limited data on WCD benefit in acute decompensated HF setting.
Methods: The Study of the Wearable Cardioverter Defibrillator in Advanced Heart-Failure Patients (SWIFT) was a prospective observational clinical trial carried out at two medical centers. Patients hospitalized with advanced HF symptoms and reduced left ventricular function were enrolled and prescribed a WCD prior to discharge for a total of 3 months. Outcome measures included arrhythmic events, WCD discharge, and death.
Results: Study patients (n=75, mean age 51±14 years, 30% women) had a mean left ventricular ejection fraction (LVEF) of 21.5±10.4%. Non-ischemic and ischemic cardiomyopathies were present in 66% and 34% of patients, respectively. The median WCD wearing time was 59 (interquartile range 17-97) days, and 80% of the patients wore the device >50% of daily hours. WCD interrogations showed a total of 7 arrhythmic events in 5 patients (7%), including 3 non-sustained or self-terminating ventricular tachycardia (VT) events, and one polymorphic VT successfully terminated by the WCD. None of the patients died while wearing the device and no inappropriate device therapies occurred. Upon termination of treatment with the WCD, 21 patients (28%) received an ICD. At 3 years the cumulative death rate was 20% in the ischemic and 21% in non-ischemic cardiomyopathy patients.
Conclusions: A management strategy incorporating the WCD can be safely used to bridge the decision regarding the need for ICD implantation in high-risk patients with advanced HF.

ABSTRACT AB09: Cryoballoon Ablation

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB09-01

THE BRONCHIAL EFFECTS OF CRYOBALLOON ABLATION FOR ATRIAL FIBRILLATION

Nishant Verma, MD, MPH, Colin T. Gillespie, MD, Albert C. Lin, MD, Todd T. Tomson, MD, Sanjay Dandamudi, MD, Paloma Pina, MD, Sukit Ringwala, MD, MPH, Alexandru B. Chicos, MD, Susan S. Kim, MD, Rishi Arora, MD, Rod S. Passman, MD and Bradley P. Knight, MD, FHRS. Northwestern University, Chicago, IL

Introduction: Damage to extracardiac structures, including the esophagus and phrenic nerve are known complications of cryoballoon ablation (CBA) during pulmonary vein (PV) isolation for atrial fibrillation (AF). Other adjacent structures, including the pulmonary bronchi and lung parenchyma may be affected during freezing of the PV ostia. The effects of cryoenergy on the pulmonary bronchi during CBA have not previously been explored.
Methods: Five patients undergoing CBA for AF under general anesthesia were enrolled in an IRB-approved prospective, observational study. Pre-procedure MRIs were used to determine the proximity between the bronchi and PVs. Patients underwent CBA using standard techniques. In PVs adjacent to pulmonary bronchi, real-time bronchoscopy was performed during cryoablation to monitor for ice formation and evidence of thermal damage.
Results: All patients were found to have a close anatomic relationship between the left upper pulmonary vein (LUPV) and the left mainstem bronchus. Two patients had close proximity of the right upper pulmonary vein (RUPV) to the right mainstem bronchus. In 3 of 5 patients and 6 of 10 freezes, ice formation was visualized during cryoablation in the LUPV (Fig. 1). Ice formation was not seen in the RUPV. The average time to ice formation was 55 seconds and the average minimum balloon temperature achieved was -50°C. No patients have developed respiratory symptoms in a mean follow up time of 3.4 months.
Conclusions: Inadvertent cryoablation can occur in the left mainstem bronchus during CBA for AF. The long-term consequences of this novel finding are unknown.

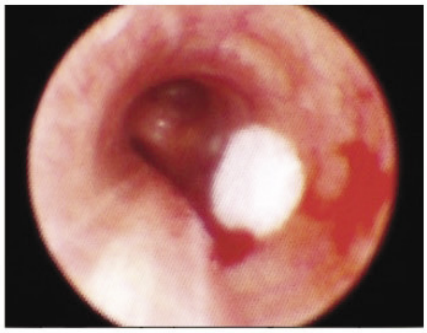
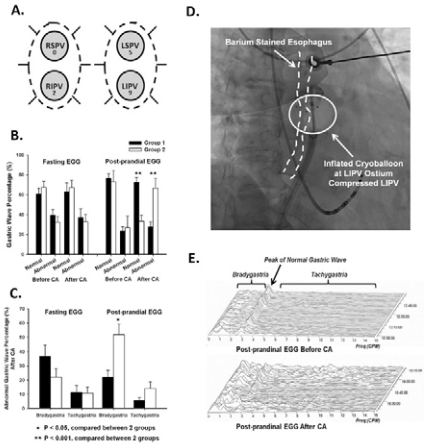


Figure 1: Ice Formation in the Left Mainstem Bronchus
Ice formation is seen in the left mainstem bronchus during cryoballoon ablation of the left upper pulmonary vein. Thawing of the lesion was seen during balloon warming.



AB09-02

PERIESOPHAGEAL VAGAL INJURY DURING FREEZING LEFT INFERIOR PULMONARY VEIN: SAFETY CONCERNS OF ATRIAL FIBRILLATION CRYOBALLON ABLATION

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Introduction: The incidence of periesophageal vagal injury (PNI) after cryoablation (CA) is higher than radiofrequency ablation. The study aimed to investigate the PNI and gastric rhythms after CA of AF.
Methods: Of consecutive 20 patients admitted for AF CA, electrogastrography (EGG) was used to evaluate gastric myoelectrical activities before and after procedure. Anatomical distribution of 4 PVs was annotated from CT scan and angiography during procedure. Group 1 consisted of the patients without compression of cryoballoon to pulmonary vein (PV) during CA, and group 2 consisted of patients with at least one PV compressed or shifted by cryoballoon during CA.
Results: Ten (50%, Group 2) patients showed compression of 1.4±0.2 PVs during CA, especially left inferior PV (LIPV, 90%, Fig A). Gastric myoelectricity was similar between the two groups before CA. After CA, the patients in group 2 showed significantly increased percentages of abnormal postprandial gastric slow wave than those in group 1. (Fig B).Increased percentage of postprandial bradygastria was mainly responsible for the gastric dysrhythmia in Group 2 (Fig C). After ablation, more patients in group 2 would be suffered from upper GI symptoms than those in Group 1 (70% vs. 20%, p=0.02). Fig D. shows an example of LIPV compression in barium stained esophagus and it caused significant gastric dysrhythmia (increasing bradygastria) after CA (Fig E).
Conclusions: Balloon compression of LIPV causes significant safety concern with symptomatic bradygastia after AF CA. Meticulous adjustment the balloon location with careful energy application is important to avoid PNI.

AB09-03

LESSONS LEARNED FROM ATRIAL FIBRILLATION CRYOABLATION LESION ASSESSMENT AND QUANTIFICATION WITH DELAYED-ENHANCEMENT MAGNETIC RESONANCE IMAGING

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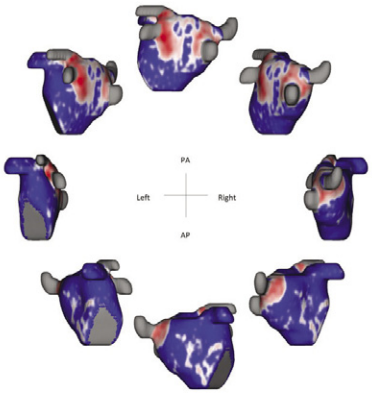
Introduction: Late gadolinium enhancement magnetic resonance imaging (LGE-MRI) identifies post ablation scar associated with catheter ablation for atrial fibrillation (AF). We hypothesize that LGE-MRI effectively identifies left atrial and esophageal injury with cryoablation and correlates to successful ablation outcome.
Methods: 25 patients with AF underwent cryoablation. All patients had a pre-ablation LGE-MRI for assessment of left atrial fibrosis and a 24 hour post-ablation DE-MRI for assessment of left atrial and esophageal injury. 17 patients underwent a 3 month post-ablation LGE-MRI for quantification of cryoablation scar. Mean follow-up was 204 ± 121.9 days. AF ablation failure was defined as atrial tachyarrhythmia > 30 seconds after a 3 month blanking period.
Results: Mean age was 60 ± 11.4 years; mean left ventricular ejection fraction was 56 ± 11.3%. Sixteen (64%) patients had paroxysmal AF; 9 (26%) had persistent AF. 6 patients had esophageal late gadolinium enhancement on 24 hour LGE-MRI. All 6 patients had a 3-month post ablation LGE-MRI without esophageal enhancement. 20 (80%) patients had clinical improvement of their AF; 11 (44%) - NO AF/AT; 9 (36%) - reduced AF burden. Three (12%) had AF without improvement. On LGE-MRI at 3 months the mean scar quantification was 26.4 ± 5.17%. 10 (59%) patients had contiguous ablation scar around each pulmonary vein (figure 1) and were free of AF or had reduced AF burden. 7 (41%) pateints had an ablation scar gap. 3 of 7 (43%) had AF recurrence with no change in AF burden. All 7 patients had an ablation scar gap around the right superior or inferior pulmonary veins.
Conclusions: Continguous scar with cryoablation is associated with AF ablation success.



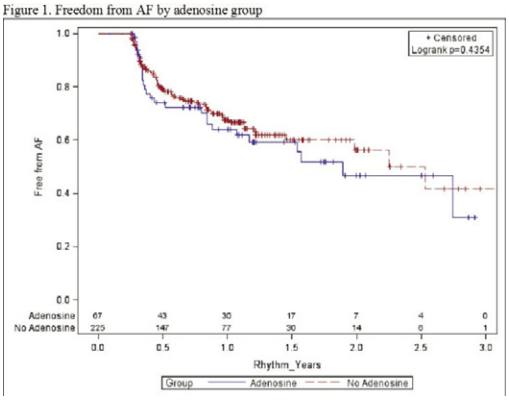
AB09-04

RECONNECTION RATE AND LONG-TERM OUTCOME WITH ADENOSINE PROVOCATION DURING CRYOBALLOON ABLATION FOR PULMONARY VEIN ISOLATION

Rachel M. Kaplan, MD, Sanjay Dandamudi, MD, Martha Bohn, RN, BSN, Nishant Verma, MD, Todd T. Tomson, MD, Paloma Pina, MD, Sukit Ringwala, MD, Rishi Arora, MD, Alexandru B. Chicos, MD, Jeffrey J. Goldberger, MD, FHRS, Susan S. Kim, MD, Bradley P. Knight, MD, FHRS, Albert C. Lin, MD and Rod S. Passman, MD. Northwestern University, Chicago, IL, Northwestern Memorial Hospital, Chicago, IL, Northwestern Univ - McGaw Medical Center, Chicago, IL, Northwestern Memorial Hospital, Dept of Cardiology, Chicago, IL

Introduction: Adenosine can be used to unmask dormant conduction during pulmonary vein isolation (PVI) for atrial fibrillation (AF). Studies of adenosine use in radiofrequency PVI have revealed high reconnection rates and conflicting results for long-term success. In contrast, reconnection rates and outcomes with adenosine for PVI with cryoballoon ablation (CBA) are poorly defined.
Methods: A prospectively maintained database of patients undergoing first CBA at a single institution was analyzed. Adenosine use was at the discretion of the primary operator. Additional freezes were delivered for reconnected veins until dormant conduction was eliminated. The primary endpoint, time to AF recurrence defined as any episode > 30 seconds after a 3-month blanking period, was assessed by Kaplan-Meier analysis.
Results: From 2011 to 2015, 406 patients underwent CBA, 361 of whom had > 3 months follow-up. The mean age was 61.7 years and 69% were male. Overall, the prevalence of paroxysmal AF was 79% with no significant difference between those that did and did not receive adenosine (77% vs 86%, respectively, p = 0.23). Adenosine testing was performed in 78 patients (21.6%) with a mean dose of 10.6 mg/vein. Of the 306 veins evaluated, 19 (6%) demonstrated dormant conduction. Over a median follow-up period of 9.4 months, there was no significant difference in freedom from AF between those that did and did not receive adenosine (p= 0.43) (Figure 1).
Conclusions: Dormant conduction with adenosine is uncommon following CBA and its use does not improve long-term success rates. Larger studies are needed to confirm these findings.

Figure 1. Freedom from AF by adenosine group

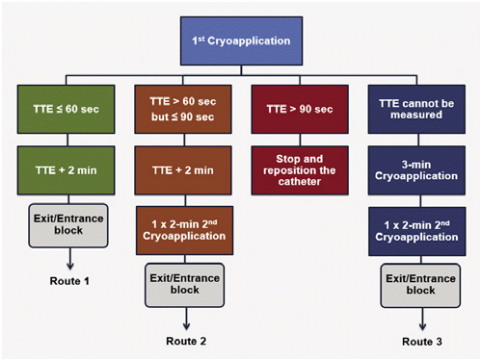


AB09-05

VERIFICATION OF A NOVEL ATRIAL FIBRILLATION CRYOABLATION DOSING ALGORITHM: ACUTE AND MID-TERM RESULTS FROM THE CRYOBALLOON-ABLATION DOSING BASED ON THE ASSESSMENT OF TIME TO EFFECT AND PULMONARY VEIN ISOLATION GUIDANCE (CRYO-DOSING) STUDY

Arash Aryana, MD, Marcin Kowalski, MD, P. Gearoid O'Neill, MD, Charles Koo, MD, Hae W. Lim, PhD, Asif Khan, MD, Robert B. Hokanson, BA, Mark R. Bowers, MD, David N. Kenigsberg, MD, Cryo-DOSING Investigators. Dignity Health Heart and Vascular Institute, Sacramento, CA, Staten Island Heart and North Shore-LIJ Health System, Staten Island, NY, Monmouth Cardiology Associates, Freehold, NJ, Medtronic, Inc, Minneapolis, MN, Staten Island University Hospital, Staten Island, NY, Florida Heart Rhythm Specialists, PLLC, Plantation, FL

Introduction: There are no recommendations on the optimal dosing of cryoablation of AF (Cryo-AF) using the current cryoballoon. This multicenter study prospectively evaluated the procedural and clinical outcomes of Cryo-AF using a pre-specified dosing algorithm guided solely by pulmonary vein (PV) isolation (time to effect, TTE).
Methods: Available data suggest that during Cryo-AF a TTE ≤60 sec is likely considered optimal, a TTE 61-90 sec acceptable, and a TTE >90 sec suboptimal in predicting acute and durable PV isolation. Consequently, we developed a Cryo-AF dosing algorithm (figure) and prospectively tested it in pts undergoing Cryo-AF.
Results: Outcomes from 348 consecutive pts undergoing a first Cryo-AF using the proposed algorithm were examined. In total, 99.6% of PVs were isolated in 98.6% of pts using a 23-mm (0.3%) or 28-mm (100%) cryoballoon (no. of applications/PV 1.7 ± 0.8, application duration 149 ± 34 s, nadir temperature -47 ± 9ºC, TTE 47 ± 16 s, thaw time 43 ± 28 s, left atrial dwell time 51 ± 14 min, fluoroscopy time 13 ± 6 min, procedure time 84 ± 24 min). Adverse events included acute procedure related events (1.1%) and persistent phrenic nerve palsy (0.6%). Freedom from AF/atrial arrhythmias was 91.8% (24/293) at 3 and 81.6% (23/125) at 6 months; 6 pts required a redo procedure (4 ± 1 months) in whom only 1/32 PVs (3.1%) exhibited reconnection. In comparison, Cryo-AF using a conventional approach in a matched cohort of 773 pts yielded longer fluoroscopy, ablation, and procedure times with similar safety and efficacy.
Conclusions: A novel Cryo-AF dosing algorithm guided by time to PV isolation yielded improved procedural endpoints with optimal short and mid-term clinical outcomes.

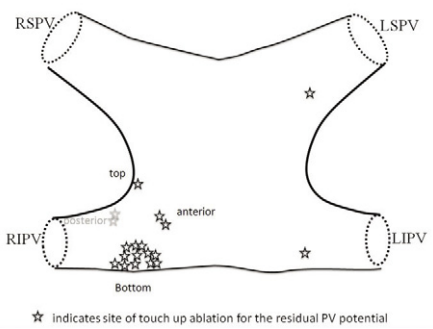


AB09-06

PULMONARY VEIN ANTRAL RE-MAPPING AFTER CRYOBALLOON ABLATION FOR ATRIAL FIBRILLATION

Kenichi Yokoyama, MD, Kenichi Tokutake, MD, Ryousuke Narui, MD, Shinichi Tanigawa, MD, Seigo Yamashita, MD, Michifumi Tokuda, MD, Keiichi Inada, MD, Seiichiro Matsuo, MD, Michihiro Yoshimura, MD and Teiichi Yamane, MD. Jikei Medical University, Tokyo, Japan

Introduction: Establishment of pulmonary vein (PV) isolation during cryoballoon ablation is generally confirmed by use of an octapolar inner-lumen mapping catheter (Achieve®, Medtronic, Minneapolis, MN, USA) which is placed distal to the cryoballoon. However, Achieve® could not completely describe the real-time PV disconnection during ablation. The aim of this study is to evaluate the incidence of the residual PV potentials detected by the conventional circular catheter after cryoballoon ablation.
Methods: 104 patients (414 PVs) with paroxysmal AF who underwent the initial cryoballoon ablation were included. After the elimination of PV potential was confirmed by Achieve®, conventional 20-30mm 20-polar circular catheter was placed at PV antrum to detect the remaining PV potentials.
Results: PV was isolated by cryoballoon in 409 PVs, except for 5 PVs which were considered as unsuitable for cryoballoon ablation due to anatomical constraints. Although the elimination of PV potential had been confirmed by Achieve®, the residual PV potential was detected by the conventional circular catheter at PV antrum in 3.2% (13/409) of PVs (left-superior in 1(1.0%), left-inferior in 2(2.0%) and right-inferior in 10(9.6%)). All those residual potentials were successfully eliminated by touch-up ablation. The site of the touch-up ablation is shown in Figure.
Conclusions: An octapolar inner-lumen mapping catheter might overlook the incomplete PV isolation during cryoballoon ablation, especially in bottom portion of right-inferior PV. Re-mapping using the conventional circular catheter is recommended to confirm the complete PV antral isolation by cryoballoon.



ABSTRACT AB10:
Lessons on the Mechanisms of AF During Ablation

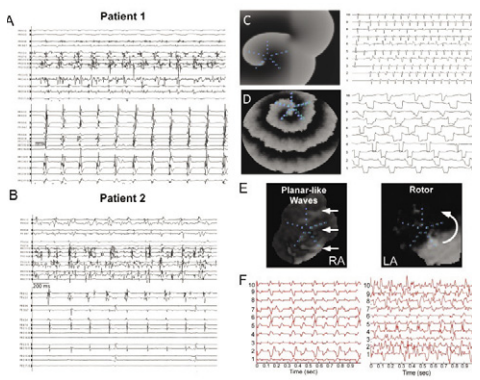
Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB10-01

CLUSTERS OF FAST AND FRACTIONATED ELECTROGRAMS ENABLE THE LOCALIZATION OF ATRIAL FIBRILLATION SOURCES PROPAGATING WITHIN A FIBROTIC ATRIAL MYOCARDIUM

Jerome Kalifa, MD, Omer Berenfeld, PhD, Clement Bars, MD, Jacques Faure, MD, Uma Mahesh R. Avula, MD, Michel Bremondy, MD, Sylvain Beurtheret, MD, Ange Ferracci, MD, Andre Pisapia, MD and Julien Seitz, MD. Center for Arrhythmia Research - University of Michigan, Ann Arbor, MI, Hospital Saint Joseph, Marseille, France, University of Michigan, Ann Arbor, MI, St. Joseph Hospital, Marseille, France

Introduction: We tested the hypothesis that clusters of fast CFAEs — but not isolated CFAEs — are indicative of localized AF sources in fibrotic atria.
Methods: 105 patients in AF were pre-mapped with a multipolar catheter (Pentarray, Biosense). Pentarray mapping enabled the tagging of regions with clusters of at least 3 contiguous fast CFAEs electrograms (“hot”). Subsequently, “hot” regions were exclusively ablated (PVs were not isolated). Then, electrograms from “hot” regions were compared with the ones recorded in non-tagged (“cold”) regions. Also, we simulated fibrillation with a human atrial model (5x5-cm, realistic atrial fibrosis distribution). After rotor initiation, multipolar electrograms were calculated for a virtual Pentarray. Finally, we used an ovine model of left atrial myocardial infarction (ligation of a left atrial coronary branch, LAMI) to conduct simultaneous right-left (RA, LA) atrium optical mapping in isolated hearts during AF (DI-4-ANEPPS, 500 fr/sec).
Results: In patients, ablation at “hot” regions led to AF termination in 100/105 patients. “Hot” (Fig: A, B; top) — but not “cold” (Fig: A, B; bottom)— regions exhibited clusters of fast CFAEs. In simulations, a virtual Pentarray yielded clusters of fast CFAEs when positioned over the center of a driver rotor (Fig: C, D) but not in a bystander wavebreak region (not shown). Similarly, the wavefront of an ovine atrial scar-anchored LA rotor yielded clusters of CFAEs. At the periphery of the rotor, impulses in the RA were planar-like and clusters of fast CFAEs were not seen (Fig: E, F).
Conclusions: Clusters of fast CFAEs — but not isolated CFAEs — are indicative of AF sources propagating within a fibrotic atrial myocardium.

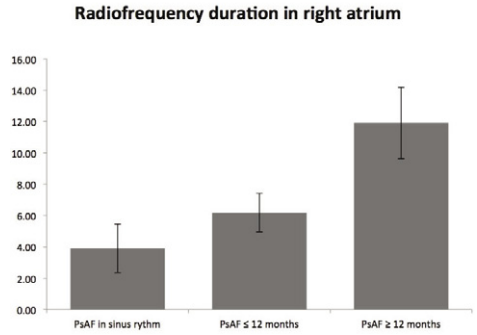


AB10-02

INCIDENCE OF DRIVERS OF PERSISTENT ATRIAL FIBRILLATION IN THE RIGHT ATRIUM

Grégoire Massoullié, MD, Nicolas Derval, MD, Ghassem Cheniti, MD, Masateru Takigawa, MD, Antonio Frontera, MD, Jean-Yves Wielandts, MD, Nathan Thompson, MD, Nora Al Jefairi, MD, Elvis Teijeira, MD, Sana Amraoui, MD, Arnaud Chaumeil, MD, Arnaud Denis, MD, Frederic Sacher, MD, Pierre Jais, MD, Meleze Hocini, MD and Michel Haissaguerre, MD. Bordeaux University Hospital, Bordeaux, France, Bordeaux University Hospital, Pessac, France

Introduction: Specific noninvasive signal processing was applied to identify right atrial (RA) drivers in distinct categories of persistent atrial fibrillation (PsAF).
Methods: In 290 consecutive PsAF patients, accurate biatrial geometry relative to an array of 252 body-surface-electrodes was obtained from non-contrast CT-scan. The reconstructed unipolar AF-electrograms acquired bedside from multiple windows (duration:13±7s) were signal-processed to identify AF drivers and their cumulative density map (focal activity, re-entrant activity). The driver domains were catheter ablated by using AF termination as the procedural end point.
Results: AF termination was obtained in 76 patients (80%) of induced AF, 95 (70%) of PsAF and 30 (51%) of long-standing PsAF. Targeted region in the RA increased with the duration of continuous AF: 32% in patients presenting in sinus rhythm (induced AF, n=95); 60% in PsAF (≤12 months; n=135) and 85% in long-lasting PsAF (>12 months; n=60) (p=0.002). Total RF delivery in RA was 4±7min, 6±7min, 12±8min, and AF termination site was the RA in 14 pts (18%), 21 pts (22%) and 8 pts (27%) in each group respectively (p<0.001). AF termination was usually a conversion to left atrial tachycardia (71%). The upper RA including the appendage was the dominant driver region (70%). Patients without AF termination (70/90) required longuer ablation in the RA (4±7min vs. 11±8min, p<0.001), suggesting that biatrial disease is associated with poorer procedural outcomes.
Conclusions: Incidence of right atrial drivers in PsAF increases with the duration of continuous AF suggesting a rapid progression to a biatrial disease and favors early therapy.



AB10-03

DETECTION OF ROTORS AND FOCAL IMPULSES USING FIRM MAPPING BASED ON A 64-POLE BASKET CATHETER IN ATRIAL FIBRILLATION PATIENTS, PITFALLS DUE TO LACK OF 3D LOCATION AND SIGNAL QUALITY

Philipp Halbfass, MD, Karin Nentwich, MD, Markus Roos, MD, Kai Sonne, MD, Attila Szöllösi, MD, Franziska Fochler, MD, Elena Ene, MD, Ruty Reich, BSc and Thomas Deneke, MD, FHRS. Heart Center Bad Neustadt, Bad Neustadt a.d. Saale, Germany, Biosense Webster Ltd., Haifa, Israel

Introduction: Focal impulse and rotor modulation (FIRM) is an ablation strategy targeting repetitive sources identified during ongoing atrial fibrillation. Until now FIRM mapped sources have not been assessed by any other mapping software. This work analyzed the FIRM locations in 3D space and with conventional electrophysiolgical criteria.
Methods: We included consecutive patients with persistent atrial fibrillation undergoing FIRM ablation. Endpoints of the study were detection of corresponding left atrial rotating repetitive patterns, organization or termination of atrial fibrillation during ablation. Patients underwent FIRM guided ablation followed by PVI. Mapping of left atrial rotors was done with a 64-pole basket catheter in conjunction with the Rhythm ViewTM mapping system. The signals of the 64-pole basket (FIRM map) were also recorded on a novel mapping system (Carto FinderTM) embedded in the 3D EAM system (Biosense Webster Inc., Diamond Bar, CA, USA). To ensure consistency of the findings, each ‚epoch“ was followed by another ‚epoch“. After this a 30sec recording was taken for 3D and electrophysiological offline analysis after the procedure.
Results: Nine patients were included in the study (male n=6; 66.5 ± 8.6 years) and 3.1 ± 1.6 left atrial rotors were identified and ablated. 31 recordings were analyzed for 3D locations and electrophysiological analysis. In 16 of the 31 recordings (52%) at least one of the intercardiac signals identified had none or extremely low voltage atrial activity. In 2 recordings (6%) the inter spine distance of the poles demarking the ablation region exceeded 2cm. Rotational activities corresponding to the FIRM identified locations were identified only in 23% of the recordings. The ratio of channels with high quality atrial signals ranges between 9% to 93% with a mean of 50% = equivalent to 32 poles only. There was no corrolation between FIRM identified locations to higher DF in the recordings.
Conclusions: In our study the RhythmView™ system identified FIRM LA sources at a rate similar to previous publications. Intercardiac signals demonstrated lack of atrial activations in more than half of the identified FIRM sources. There was no correlation between any FIRM identified location to higher Dominanf Frequency.

AB10-04

IMPACT OF ACUTE ATRIAL FIBRILLATION TERMINATION AND PROLONGATION OF AF CYCLE LENGTH ON THE OUTCOME OF ABLATION OF PERSISTENT AF: A SUB-STUDY OF THE STAR AF II TRIAL

Simon Kochhäuser, MD, Chenyang Jiang, MD, Timothy R. Betts, MD, Jian Chen, MD, Isabel V. Deisenhofer, MD, Roberto Mantovan, MD, Laurent Macle, MD, Carlos A. Morillo, MD, FHRS, Wilhelm Haverkamp, MD, Rukshen Weerasooriya, MD, Jean-Paul Albenque, MD, Stefano Nardi, MD, PhD, Endrj Menardi, MD, Paul G. Novak, MD, Prashanthan Sanders, MD, PhD and Atul Verma, MD, FHRS. University Hospital Münster, Münster, Germany, Zhejiang Shaoyifu Hospital, Hangzhou, China, Oxford University Hospitals NHS Trust, Oxford, United Kingdom, Haukeland Univ Hospital, Bergen, Norway, Deutsches Herzzentrum Muenchen, Munich, Germany, Ospedale Regionale, Treviso, Italy, Montreal Heart Institute, Montreal, QC, Canada, Hamilton Health Sciences - McMaster University, Hamilton, ON, Canada, Medizin. Klinik Schwerpunkt Kardiologie, Berlin, Germany, Royal Perth Hospital, Perth, Australia, Clinique Pasteur, Toulouse, France, Presidio Ospedaliero Pineta Grande, Castel Volturno (CE), Italy, Azienda Ospedaliera S. Croce e Carle, Cuneo, Italy, University of Adelaide and Royal Adelaide Hospital, Adelaide, Australia, Southlake Regional Health Centre, Newmarket, ON, Canada

Introduction: There is controversy about the impact of

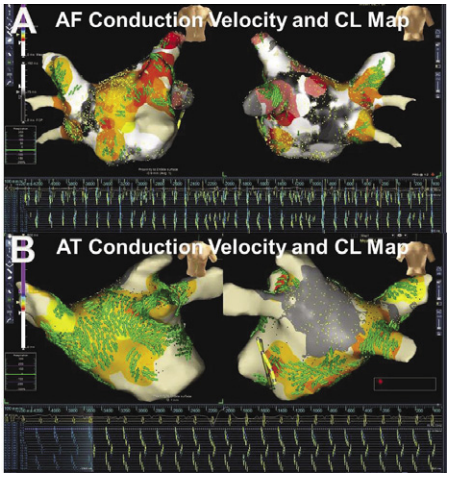
acute atrial fibrillation (AF) termination and prolongation of AF cycle length (AFCL) acutely during ablation on the long-term procedural outcome. We analyzed the influence of AF termination and AFCL-prolongation on freedom from AF in patients from the STAR-AF II trial.
Methods: STAR-AF II was a large, multicenter trial randomizing 589 patients with persistent AF to different ablation strategies. Acute changes in AFCL and AF termination were collected during the index procedure and both were compared to recurrence of AF at 18 months. Recurrence was defined as AF > 30 seconds based on ECG, Holters (3,6,9,12,18 months), and weekly transtelephonic monitor ECGs for 18 months. The impact of AF termination was also compared to other predictors of procedural outcome by Cox regression analysis.
Results: AF terminated in 8% of the pulmonary vein isolation (PVI) arm, 45% in the PVI+complex electrogram arm, and 22% of the PVI+linear ablation arm (p<0.001) but the 18 month freedom from AF did not differ between the 3 groups (p=0.15). Freedom from AF at 18 months was significantly higher in patients who presented to the lab in sinus rhythm compared to those who presented in AF but did not terminate during ablation (63% vs. 44%; p=0.007). Those who presented in AF but terminated during ablation had an intermediate outcome (53% AF freedom at 18 months) but this was not significantly different from either those in sinus (p=0.84) or those who did not terminate (p=0.08). AF termination was a univariable predictor of success at 18 months (p=0.007) but by multivariable analysis, performing PVI predominantly during sinus rhythm was the strongest predictor (HR 1.80, p<0.001). Prolongation of the AFCL was not predictive of 18 month freedom from AF.
Conclusions: Acute AF termination and prolongation in AFCL did not predict 18 month freedom from AF. Performing PVI predominantly during sinus rhythm was the strongest predictor and could explain better outcome in patients with early AF termination during ablation.

AB10-05

REAL-TIME ELECTROPHYSIOLOGICAL MAPPING OF CONSISTENT WAVE FRONT PROPAGATION DURING ATRIAL FIBRILLATION AND ATRIAL TACHYCARDIA

Carlo Pappone, MD, PhD, Massimo Saviano, MD, Giuseppe Ciconte, MD, Wenwen Li, PhD, Erhan Erdemir, PhD, Amarild Cuko, MD, Luigi Giannelli, MD, Manuel Conti, MD, Gabriele Vicedomini, MD and Vincenzo Santinelli, MD. IRCCS Policlinico San Donato, San Donato Milanese, Italy, St. Jude Medical, Sunnyvale, CA, St. Jude Medical, St Paul, MN

Introduction: Real-time electrophysiological wave front mapping during atrial fibrillation (AF) and atrial tachycardia (AT) might be valuable for understanding of arrhythmia mechanisms. The aim of this study is to identify and characterize consistent wave fronts during AT/AF.
Methods: Consecutive patients with AT/AF (both paroxysmal and persistent AF) undergoing catheter ablation were enrolled. All procedures were preceded by electroanatomical mapping (EAM) using Inquiry™ AFocus II™ catheter. A novel mapping software (EnSite™ Velocity™ Research Software) was used retrospectively to analyze consistency index (CI) of wave fronts for a minimum length of 5 seconds. Cycle length (CL), conduction velocity (CV), and bipolar voltage of wave fronts that had CI ≥ 50% were analyzed.
Results: In the 37 patients enrolled, EAM was acquired during AF in 29 pts (78%) and AT in 8 pts (22%). In the AF maps, regions with consistent (CI ≥ 50%) wave fronts accounted for 12 ± 8% of left atrium surface area. Rotational wave fronts were observed in 10 of 109 (9%) regions in 7 of 29 (24%) patients. In 8 AT maps, a total of 7 reentrant circuits and 1 focal activity were identified. As shown in Fig A-B, CV is represented by 3D green arrow and CL is color coded. As compared to AT maps, the consistent wave fronts during AF had shorter CL (179 ± 30 vs 235 ± 30 ms, p<0.001) and slower CV (0.44 ± 0.05 vs 0.55 ± 0.08 m/s, p<0.001). However, the peak-peak voltage of consistent wave fronts was similar in both groups (0.96 ± 0.34 vs 1.05 ± 0.39 mV, p=0.6).
Conclusions: Consistent wave front propagation during AT/AF can be successfully identified and characterized. Conduction velocity of wave front decreases along with faster cycle length.



AB10-06

ELECTROGRAM CHARACTERISTICS OF TERMINATION SITES IN PERSISTENT ATRIAL FIBRILLATION

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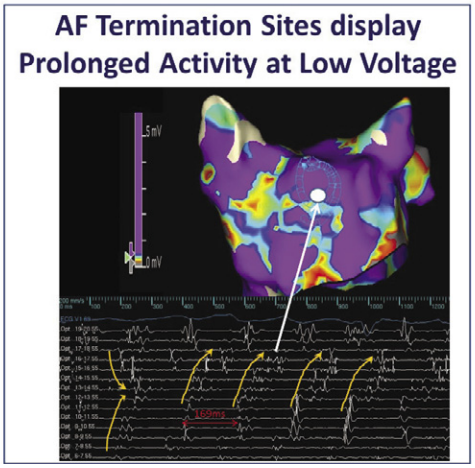
Introduction: Non-PV focal and rotational sources may cause persistent AF. We assessed regional EGM characteristics (activation pattern, voltage, consistency) at AF termination sites.
Methods: 32 patients with PsAF underwent high-density mapping prior to PVI and low voltage-based ablation. EGMs of 15 consecutive AF beats were assessed at AF termination sites for: 1) regional activation patterns & consistency on 20-pole catheter 2) AF cycle length (AFCL) 3) duration of electrical activity. EGM voltages were compared between mapping-catheter and ablation-catheter (1mm vs. 3,5mm tip, 5mm vs 3mm spacing).
Results: AF terminated in 3/32 during PVI, in 29/32 by selective ablation of low voltage areas. RF duration beyond PVI was 11+/-10 min. AF termination sites displayed prolonged electrical activity >70% AFCL on 20-pole catheter. These patterns were repeatedly observed in clusters (2.5 beats, range 2-5 consecutive beats). Prolonged activity >50% AFCL was found in all patients on a single bipole. All termination sites were within / at borderzones (<10mm) of low voltage areas <0.5mV. Bipolar voltage at AF termination sites were significantly higher on the 20-pole catheter vs ablation catheter (0.48+-0.17mV vs 0.22+/-0.17, p<0.001).
Conclusions: AF termination sites display specific regional activation and voltage characteristics. Multielectrode-mapping reveals rapid focal or rotational activity at low voltage<0,5mV in

majority (80%) of cases. The catheter design influences bipolar voltage and the ability to identify active driver sites.



ABSTRACT PLUS AB11:
Atrial Fibrillation and Left Atrial Tachycardia Novel Mapping and Ablation Techniques

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB11-01

COMBINATION OF LEFT ATRIAL APPENDAGE CLOSURE WITH CATHETER ABLATION FOR THE TREATMENT OF ATRIAL FIBRILLATION

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Introduction: Catheter ablation could not eliminate risks of stroke absolutely in patients with atrial fibrillation (AF). Left atrial appendage closure (LAAC) had showed benefits in prevention of stroke in patients with AF. This study was to evaluate the safety and efficacy of combination of LAAC with catheter ablation for the treatment of AF.
Methods: Twenty-two patients (M,13) with persistent AF were enrolled into this study, with a mean age of (78.9±4.7)y. The history of AF was (5.3±3.9)y. All the patients had a history of stroke (from transient ischemia attack to hemiplegy). While transesophageal echocardiography confirmed there were no left atrial thrombus in all the patients 72h before procedure. Circumferential pulmonary vein isolation plus roof line and mitral isthmus line ablation were performed in all the patients. After that, LAAC were performed with Lefort Closer device (Lepu, Beijing, China) in the same procedure. Oral warfarin with aspirin and clopidogrel were taken at 45 days after procedure. Then aspirin and clopidogrel were taken till 6 months. After that, oral aspirin was maintained.
Results: All patients had been performed catheter ablation with LAAC. With a mean duration of (10.9±3.2) months, 15 patients maintained sinus rhythm. No stroke was observed among the patients. There was no case of severe procedure related complications.
Conclusions: This study showed the feasibility and efficacy of combination of LAAC with catheter ablation for the treatment of AF in patients with high risks of stroke.

AB11-02

MULTIFUNCTION FIBRE OPTIC CATHETER FOR ATRIAL FIBRILLATION TREATMENT

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Introduction: Catheter ablation is a validated therapy for most arrhythmias including AF. However, safety and efficacy could be dramatically improved by using lesion formation and depth monitoring during energy delivery.
Methods: An entirely all-optical 2.8mm-diameter multifunction fibre-optic catheter for AF treatment was developed, to perform laser ablation and tissue depth monitoring, simultaneously. Ex-vivo Experiments (chicken heart) were carried out to demonstrate fast and accurate tissue ablation as well as in-situ optical coherence tomography (OCT) of ablated tissues. The catheter was placed perpendicularly to the tissue in the tissue prep shown in the figure. Different power and duration settings were assessed to reach consistently a 2-3 mm depth which would accommodate most of the atrial lesions for AF ablation.
Results: Using a laser pulse power of 7 Watts for 10 seconds lesion depth was 2.6±0.3 & diameter 3.15±0.4 mm. Importantly, OCT showed clear tissue changes online visible on the first mm of tissue depth.
Conclusions: This 2.8mm-diameter multifunction fibre-optic catheter could be suitable for AF ablation by enabling fast and accurate tissue ablation as well as in-situ tissue depth and lesion monitoring.

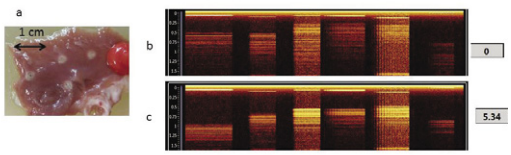

Fig. (a) Laser lesions on the chicken heart. (b) OCT signal before ablation. (c) OCT signal after ablation with increased signal intensity

AB11-03

THE EFFICACY OF MULTIPOLAR BASKET CATHETERS IN MAPPING THE ENTIRE LEFT ATRIUM IN HUMAN PERSISTENT ATRIAL FIBRILLATION

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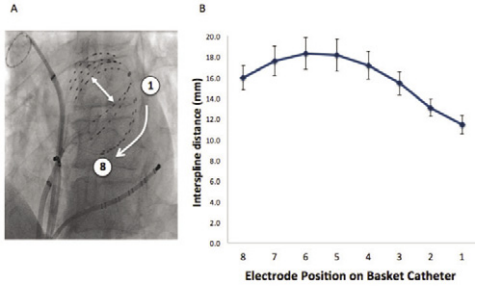
Introduction: Novel methods of mapping the human left atrium (LA) in atrial fibrillation (AF) include the multi-electrode basket catheter which allows simultaneous electrogram acquisition. However, the efficacy of this catheter in providing adequate electrode contact and electrogram recordings of the entire LA is unclear.

Methods: LA mapping was performed in 12 patients using the 56 bipolar electrode Boston Scientific Constellation catheter. Appropriate basket size was chosen based on pre-procedural cardiac CT and intra-procedural TOE. We analyzed specific spatial characteristics of the basket catheter and in particular its ability to provide global LA mapping for AF mapping including 1. Number of electrodes within 2 mm of the endocardial surface 2. Number of electrodes with suitable signal quality 3. Percentage of LA mapped 4. Interspline distance (distance between adjacent splines, figure, panel A).
Results: 12 patients were studied. 60mm basket catheters were used in 3 (25%) patients, 48mm catheters in 8 (67%) and 38mm catheter in 1 patient. In 50% of patients, Agilis sheath was used for basket catheter positioning. Mean number of electrodes within 2mm of the endocardial surface was 29±3 (45%). Of the 56 bipolar electrograms, mean of 28±7 (48%) had suitable signal quality to allow annotation for activation times. The mean percentage of LA mapped was 20.3%. There was marked variability in inter-spline distance. The greatest inter-spline distance was at the equator (19.3±1.2mm) with the least at the distal pole (12.4±0.9mm) (Figure, panel B).
Conclusions: The multipolar basket catheter provides limited coverage of the LA with poor signal quality and contact with the endocardial surface.



Panel A. The interspline distance as shown in the white arrow is the distance between adjacent splines. The basket catheter labelled such that the electrode closest to the distal pole is numbered 1 and consecutively numbered up to 8 as you move towards the proximal pole. **Panel B.** This graph shows the mean interspline distance according to the position of the electrode on the basket catheter. This graph highlights the marked variability in the interspline distance of the basket catheter

AB11-04

OVERDRIVE-PACING MAPPING - A NOVEL TECHNIQUE FOR MAPPING SCAR ASSOCIATED LOCALIZED ATRIAL TACHYCARDIA

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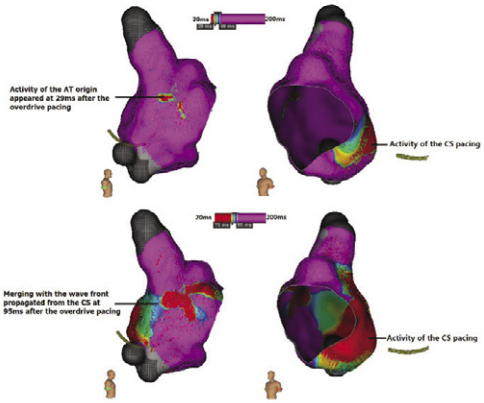
Introduction: The scar associated localized atrial tachycardia (AT) involves small part of atrium. The overdrive pacing (OP), without terminating tachycardia, can capture the tissue not critical to the tachycardia. We attempt to use this mechanism to design a new mapping technique.
Methods: Ten ATs in eight consecutive patients were studied. All patients had prior cardiac surgery and/or had prior Afib ablation. The mechanism of macro-reentrant around tricuspid or mitral annulus was ruled out. Rhythmias and Carto mapping system were used. The activation mapping was conducted during overdrive pacing with cycle length 20ms shorter than the one of AT. The AT was confirmed to persist by the same cycle length resumed after the OP discontinued.
Results: In all 10 ATs, there were localized activities independent from the sites of OP. They appeared at 62.4+/- 34.0 ms after OP and lasted for 87.4+/- 54.7 ms until merging with the wave front propagated from the OP (Figure). These activities were confirmed to be critical to the tachycardia by entrainment and the termination of the tachycardia by ablation at the area. All ATs couldn't re-induced had no recur during follow up (1-4 months). In contrast, by using conventional activation mapping, only 4 ATs were successfully located.
Conclusions: Our preliminary study demonstrated the OP mapping can be a new technique for mapping scar associated localized AT.

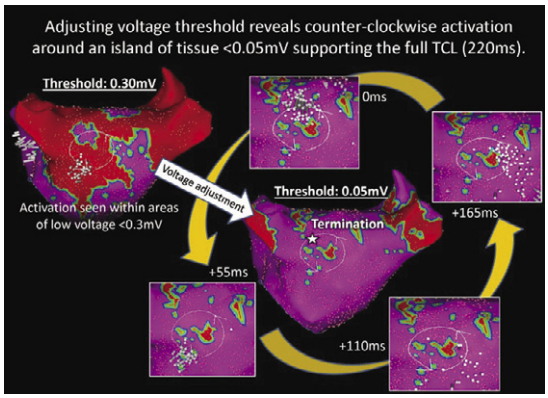


AB11-05

COMPLEX FRACTIONATED ELECTROGRAM ABLATION MAY LEAD TO SMALL LOOP ATRIAL TACHYCARDIA CIRCUITS IDENTIFIED WITH RIPPLE MAPPING

Vishal Luther, MRCP, Michael Koa-Wing, MBBS, PhD, Shahnaz Jamil-Copley, MBBS, PhD, Phang Boon Lim, MBBS, PhD, Norman A. Qureshi, MRCP, Fu Siong Ng, MD, PhD, Sajad A. Hayat, MBChB, Zachary I. Whinnett, MBBS, D. Wyn Davies, MD, FHRS, Nicholas S. Peters, MBBS, PhD, Prapa Kanagaratnam, MD, PhD and Nick Linton, MBBS, PhD. Imperial College Healthcare, London, United Kingdom

Introduction: CFE lesions can create low-voltage substrate for future reentry. We hypothesized that a composite display of activation and voltage on a single map may facilitate AT mechanism identification: Ripple Mapping was used prospectively to compare tachycardias in patients with or without prior CFE.
Methods: 34 consecutive AT pts with prior AF ablation were studied. High-density maps were created with multipolar catheters and CARTO3v4 ConfiDENSE (1841±1232 points). Ripple Mapping visualized activation as dynamic bars across a bipolar voltage map, using a voltage threshold below which no activation was seen. AT mechanism was inferred from the map and site of termination.
Results: CFE ablation had been performed in 16/34 (47%) pts and they had larger areas of low voltage (<0.3mV, CFE 37±23cm2 vs non-CFE 18±17cm2, p=0.01). AT mechanism was dependent upon PV reconnection or macro-reentry in 17/18 (95%) non-CFE pts, but only 9/16 (56%) CFE pts (p=0.01). In the other 7/16 CFE pts, small-loop reentry was fully identified in 4/7: low amplitude activity encircled small areas of very low voltage (6±2cm2; 0.12±0.06mV) encompassing the full cycle length. In the other 3/7 pts, activation broke out from a very low voltage area (0.16±0.06mV): the likely mechanism was small-loop reentry but voltages were too low to map activation. Ablation within the small loop or site of breakout terminated each AT.
Conclusions: Previous CFE ablation is associated with small loop circuits or breakout involving areas of very low voltage. These can be identified with Ripple Mapping.



ABSTRACT PLUS AB12:
Assessment of the Arrhythmogenic Substrate in Ventricular Tachycardia: Latest Developments

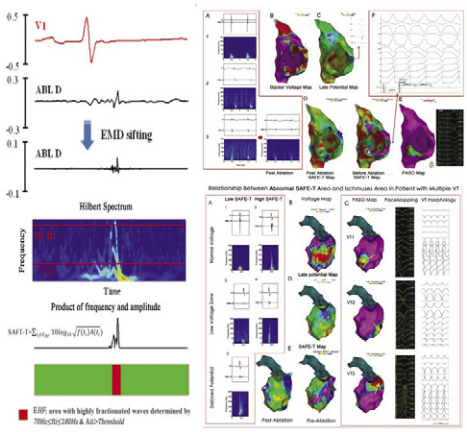
Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB12-01

SIMULTANEOUS AMPLITUDE FREQUENCY ELECTROGRAM TRANSFORMATION (SAFE-T) MAPPING TO IDENTIFY VENTRICULAR TACHYCARDIA ARRHYTHMOGENIC POTENTIALS IN SINUS RHYTHM

Yuan Hung, MD, Chin-Yu Lin, MD, John Silberbauer, MBBS, Yenn-Jiang Lin, MD, Men-Tzung Lo, PhD, Chen Lin, PhD, Hsiang-Chih Chang, PhD, Shih-Lin Chang, MD, Li-Wei Lo, MD, Yu-feng Hu, MD, Fa-Po Chung, MD, Jo-Nan Liao, MD, Chun-Wang Chiou, MD, Shih-Ann Chen, MD and Paolo Della Bella, MD. Tri-service General Hospital, Taipei City, Taiwan, Taipei Veterans General Hospital, Taipei City, Taiwan, Eastbourne General, Eastbourne, United Kingdom, Taipei Veterans General Hospital, Taipei, Taiwan, Research Center for Adaptive Data Analysis, National Central University, Jhongli City, Taiwan, National Central University, Chung-Li, Taiwan, Research Center for Adaptive Data Analysis, Jhongli, Taiwan, Taipei Veteran General Hospital, Taipei, Taiwan, Taipei Veterans General Hospital/National Yang-Ming University, Taipei, Taiwan, Ospedale San Raffaele, Milano, Italy

Introduction: Substrate ablation is useful for patients with scar-related hemodynamically unstable ventricular tachycardia (VT). We developed a novel automated technique, Simultaneous Amplitude Frequency Electrogram Transformation (SAFE-T), to identify VT isthmuses by analysis of sinus rhythm arrhythmogenic potentials (APs).
Methods: High-density ventricular mapping was performed in 3 groups: (1) 18 normal heart controls (2) 10 ischemic and (3) 8 non-ischemic VT patients. In VT patients, isthmus sites were characterized using entrainment responses. Sinus rhythm RV/LV endocardial and epicardial electrograms underwent Hilbert-Huang spectral analysis and were displayed as 3D SAFE-T maps. APs and their relation to the VT isthmus sites were studied.
Results: APs were defined by a cutoff value of 3.08 Hz-mV using normal heart controls. Receiver operating characteristics showed that VT isthmus sites were best identified using SAFE-T mapping ($p<0.001$) as compared to bipolar and unipolar scar and late potential mapping with an optimal cutoff value of 3.09 Hz-mV, allowing identification of 100% of the 34 mapped VT isthmuses, compared to 68% using late potentials. There was no significant difference between SR and paced SAFE-T values. Abnormal SAFE-T areas involved about one-quarter of the scar total area.
Conclusions: Automated electrogram analysis using 3D SAFE-T mapping allows rapid and objective identification of APs that reliably detect VT isthmuses. The results suggest that SAFE-T mapping is good alternative strategy to late potential mapping in identifying VT isthmuses and allows reduced ablation as compared to scar homogenization.



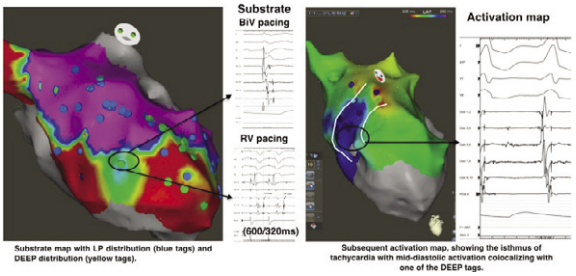
AB12-02

DECREMENT EVOKED POTENTIAL (DEEP) MAPPING: CLINICAL VALIDATION OF LIMITED SUBSTRATE ABLATION STRATEGY FOR VENTRICULAR TACHYCARDIA

Andreu Porta-Sanchez, MD, Nicholas M. Jackson, MD, Sigfus Gizurarson, MD, PhD, Atif Al-Qubbany, MD, Stéphane Massé, MEng, Marjan Kusha, MEng, Krishnakumar Nair, MD, Andrew C. Ha, MD, Eugene Downar, MD and Kumaraswamy Nanthakumar, MD, PhD. Division of Cardiology. University Health Network., Toronto, ON, Canada, John Hunter Hospital, Newcastle, Australia, Toronto General Hospital, Toronto, ON, Canada, University Health Network, Toronto, ON, Canada, Toronto General Hospital, Cardiology and Electrophysiology, Toronto, ON, Canada, Toronto General Hospital, University Health Network, Toronto, ON, Canada

Introduction: Substrate modification of VT can lead to prolonged and tedious procedures targeting a broad area of myocardium. Only a fraction of this myocardium may be actually linked to initiation and perpetuation of VT. We recently described the basis of DEEP mapping. Here we hypothesized that identification of DEEP potentials would provide a focused method for substrate based VT ablation.
Methods: Eleven male patients (14 VTs), 68.5±8.3yo, referred for VT ablation were prospectively enrolled. Nine patients had ischemic cardiomyopathy (ICM). Mean LVEF=26.4±14.6%. During substrate mapping fractionated and late potentials (LPs) were tagged and an extrastimulus was performed from the RV apex to determine which local potentials displayed decrement (DEEPs). The critical isthmus (CI) for each VT was determined if possible by activation mapping with entrainment and/or pacemapping.
Results: Mean number of points was 369 range [160-600]. Areas with LPs comprised 24.3±19.3 % of the myocardium, whereas areas with DEEPs comprised 6.7±3.5% ($p<0.05$). Mean sensitivity of DEEPs for identifying the CI of VT was 51.2%. The mean positive predictive value and specificity of DEEPs for identifying the CI was 47.4% and 95.7% respectively ($p<0.05$). Accuracy of the DEEP points for identifying the CI was 92.6% vs 74.3% for LP ($p<0.05$). The mean total procedure time was 224±72min.

Conclusions: Identification and targeting DEEP potential is feasible in the EP lab and identifies limited regions critical to the VT circuit more accurately than LPs only. DEEP-based limited substrate modification, may enable greater access to ablation for patients requiring invasive VT therapy.



AB12-03

SUBSTRATE CHARACTERIZATION AND CATHETER ABLATION OUTCOMES OF VENTRICULAR ARRHYTHMIAS IN LAMIN A/C CARDIOMYOPATHY: INSIGHTS FROM A MULTI-CENTRE STUDY

Saurabh Kumar, MBBS, PhD, Alexander Androulakis, MD, Jean-Marc Sellal, MD, Philippe Maury, MD, Estelle Gandjbakhch, MD, Xavier D. Waintraub, MD, Anne Rolin, MD, Pascale Richard, MD, Phillippe Charron, MD, Ciorsti Macintyre, MD, Katja Zeppenfeld, MD, PhD, Frederic Sacher, MD, Neal K. Lakdawala, MD, William G. Stevenson, MD, FHRS and Usha B. Tedrow, MD, MSc. Brigham & Women's Hospital, Boston, MA, Leiden University Medical Centre, Leiden, Netherlands, CHU Nancy, Vandoeuvre, France, Toulouse University Hospital, Toulouse, France, Hôpital Pitié-Salpêtrière, Département de Cardiologie, Paris, France, Cardio-myogenetic, Department of Biochimie and INSERM U582, University Hospital Pitié-Salpêtrière, Paris, France, Centre de Référence Maladies Cardiaques Héréditaires, ICAN; Inserm UMR_1166, Hôpital Pitié-Salpêtrière, Paris, France, Leiden University Medical Center, Leiden, Netherlands, Bordeaux University Hospital / LIRYC institute, Bordeaux, France, Brigham and Women's Hospital, Boston, MA

Introduction: Lamin A/C (LMNA) cardiomyopathy is a genetic disease characterized by progressive atrioventricular block (AVB), ventricular dysfunction and ventricular arrhythmias (VA). The substrate for VA in this population is not well understood.
Methods: Consecutive patients from 4 centers who had catheter ablation for sustained monomorphic ventricular tachycardia (VT) were reviewed. Clinical, electrophysiologic features, acute procedural results and outcomes are reported.
Results: 25 patients (mean age 55±9 years, 23 males, mean ejection fraction 34±12%) underwent ablation for drug-refractory VT after failing median 2 anti-arrhythmic drugs (VT storm in 36%). Any form of AVB was present in all but 2 patients (complete AVB in 11); 3 patients were on ventricular assist devices for severe heart failure. A mean of 3.8±3.2 VTs were observed per patient with mapping consistent with origin from within low voltage scar in the basal LV septum followed by the basal inferior wall and/or the sub-aortic mitral continuity. After a median of 2 procedures /patient including transcoronary alcohol in 6 and surgical cryoablation in 2), complete success (non-inducibility of any VT) was achieved in only 25% of patients and partial success (non-inducibility of at least one clinical VT) in 50%. Persistent inducibility of clinical VT was attributed to intramural septal substrate in 73% of patients. Complications occurred in 25% of patients. By 7 months after the last procedure, 91% experienced at least one recurrence, 44% were receiving or planned for transplant or mechanical support and 26% had died.
Conclusions: Basal septal scar is the main cause of VT in LMNA cardiomyopathy. Arrhythmia control is extremely challenging, often due to intramural VT origin. Onset of drug-refractory VA may be a harbinger of need for ventricular assist device or transplant in this population.

AB12-04

SUBSTRATE MAPPING FOR SCAR RELATED VENTRICULAR TACHYCARDIA IN PATIENTS WITH RESYNCHRONIZATION THERAPY - THE IMPORTANCE OF THE PACING MODE

Samuel H. Baldinger, MD, Saurabh Kumar, MD, PhD, Akira Fujii, MD, Jorge Romero, MD, Laurence M. Epstein, MD, FHRS, Gregory F. Michaud, MD, FHRS, Usha B. Tedrow, MD, FHRS, Roy M. John, MD, PHD, FHRS and William G. Stevenson, MD, FHRS. Brigham and Women's Hospital, Boston, MA

Introduction: Late Potentials (LPs) defined as electrograms (EGMs) recorded after the inscription of the surface QRS complex are associated with critical isthmuses for some scar related reentrant VTs and are a target for catheter ablation (CA). We hypothesized that in cardiac resynchronization therapy (CRT) the pacing mode (biventricular- (BiV), right-ventricular- (RV), or left-ventricular- (LV) pacing), which influences the ventricular activation sequence, would affect the detection and classification of LPs.
Methods: In consecutive patients with CRT-devices undergoing CA for scar related left ventricular VT a substrate map was created during BiV pacing using an electro-anatomic mapping system and a multipolar, multispline catheter. The catheter was then positioned in an area with abnormal EGMs and the device was programmed to LV and then to RV pacing with the catheter in the same location. A complete remap was then created during RV-pacing.
Results: In 8 males (age: 72 ± 9 years, LVEF: 25 ± 5%) a mean of 538 ± 342 electroanatomic points per map were acquired. The mean QRS duration (stimulus to end of QRS) increased from 193 ± 16ms during BiV to 256 ± 36ms during RV and 271 ± 25ms during LV pacing ($p<0.001$). EGMs were recorded at the same 36 selected sites in all three pacing modes. At 22 (61%) of these sites a LP was present during BiV pacing. LV or RV pacing unmasked a LP at 7 sites (19%). With LV pacing an EGM classified as LP during BiV pacing now fell within the QRS because of increased QRS duration at 17 sites (47%). Compared to BiV pacing, the time from the stimulus to the EGM increased with RV pacing by 26 ms ($p<0.001$) and with LV pacing by 29 ms ($p<0.001$). On average 10% of sites within the bipolar low voltage area (<1.5mV) showed a LP during BiV pacing, compared to 17% during RV pacing ($p=0.047$).
Conclusions: The pacing mode influences LP detection and classification during substrate mapping. Although LV or RV pacing delays EGMs at some sites, an increase in QRS-duration results in some LP EGMs detected during BiV pacing falling within the QRS during single chamber pacing. Further studies are needed to define the optimal pacing mode for substrate mapping according to scar location and to determine the relation to ablation outcome.

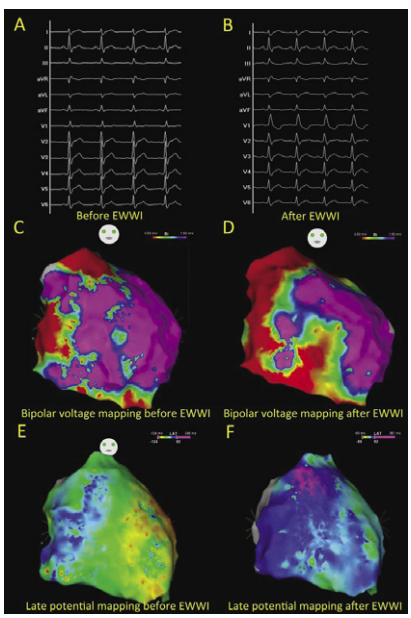
AB12-05

THE NOVEL METHODS IN ENHANCING EPICARDIAL FUNCTIONAL SUBSTRATES IN BRUGADA SYNDROME: THE ROLE OF EPICARDIAL WARM WATER INSTILLATION

Fa-Po Chung, MD, Yenn-Jiang Lin, MD, Shih-Lin Chang, MD, Li-Wei Lo, MD, Yu-feng Hu, MD, Ta-Chuan Tuan, MD, Tze-Fan Chao, MD, Jo-nan Liao, MD, Chin-Yu Lin, MD and Shih-Ann Chen, MD. Taipei Veterans General Hospital, Taipei,

Taiwan, Taipei Veterans General Hospital/National Yang-Ming University, Taipei, Taiwan

Introduction: Fever has been known to trigger ventricular tachyarrhythmias in patients with Brugada syndrome (BrS). We postulated the epicardial warm water instillation could unmask the critical epicardial substrates responsible for the arrhythmogenesis in BrS.
Methods: From 2012 to 2015, a total of 14 patients with BrS (age: 41.9±10.5; 14 male) who experienced recurrent VT/VF undergoing catheter ablation were consecutively enrolled. Epicardial warm water instillation (EWWI) was performed in 6 of 14 patients without BrS phenotype (38-39°C). Baseline ECG, repeated electroanatomical mapping, and inducibility by programmed stimulation were compared after epicardial warm water instillation.
Results: EWWI augmented and unmasked type 1 BrS phenotype in all patients (Figure A and B). Epicardial functional low voltage zone/scar increased from 87.9±46.3 cm2 to 109.6±40.6 cm2 (P=0.01; Figure C and D) after EWWI, while late potential area increased from 10.4±1.5 cm2 to 26.4±14.3 cm2 (P=0.04; Figure E and F), which decreased to 5.2±0.7 cm2 (P=0.02) after the cold water (20-22°C) instillation (Figure 1). EWWI prolonged total RV epicardial activation from 177.7±64.0 ms to 274.7±85.5 (P=0.01; Figure E and F), which could be shortened by cold water instillation. Inducibility of VT/VF increased from 16.7% to 100% (P=0.02) after EWWI. Ablation by targeting the enhanced abnormal substrates rendered noninducibility of VT/VF in all patients after repeated challenging.
Conclusions: Epicardial warm water could augment and unmask BrS phenotype and enhance the functional substrates responsible for the arrhythmogenesis ventricular tachyarrhythmias.



ABSTRACT PLUS AB13:
It›s Not Over With the Closure: Long Term Results and Protean Effects of LAA Ligation

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB13-01

DOES LEFT ATRIAL APPENDAGE EXCLUSION USING AN EPICARDIAL SYSTEM REDUCE SYSTEMIC BLOOD PRESSURES? - THE DAWN OF A NEW FRONTIER

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Introduction: Hypertension causes significant systemic and cardiovascular morbidity and mortality. While pharmacologic agents are helpful, renovascular interventions had mixed results. LAA is a unique cardiac vestige and is an integral part of Renin Angiotensin Activation System. We hypothesized that LAA elimination using a clip (Atriclip), suture ligation (Lariat) and or surgical excision in patients with atrial fibrillation could potentially down regulate the RAAS and result in lower BPs.
Methods: In this observational study 186 consecutive patients with AF (71% men; age 73±6; CHAD2 2.8±1.6; HASBLED 3.8±1.6;) who underwent successful successful epicardial LAA exclusion (Lariat - 135, Atriclip-30, Surgical excision-21) were enrolled. Heart rates and blood pressures were recorded at baseline in the clinic setting, pre surgery, post surgery @ discharge, @ 3 and 12 months.
Results: There was a significant decrease in mean SBP and DBP in the group from baseline to 24hr,3mon and 12 mon post procedure. Mean AntiHTNsive drugs decreased from 3±1 to 1.6±0.4 (p<0.01) at 56% decrease in the dosing of each. hypotensive response was seen 16-24 hours post procedure in more than 75% of patients undergoing procedure. 6% developed mild renal insufficiency at 24 hours and complete resolution subsequently.
Conclusions: LAA exclusion in patients with AF and known HTN results in significant BP reductions and the need for antihypertensive drugs. We should study this therapy for multi drug resistant HTN pts.

Variable	Baseline	Pre procedure	24 hr Post	3 mon Post	12 months Post	p-value
Heart rate	76±9	80±12	85±8	75±11	78±10	N
SBP	141.0±15.9	145±13	119±15	118±10	120±12	<0.001
DBP	80.4±12.8	70.1±11.3	70.1±11.3	70.3±11.2	71±14	<0.001

AB13-02

BLOOD PRESSURE CONTROL FOLLOWING LARIAT LAA LIGATION

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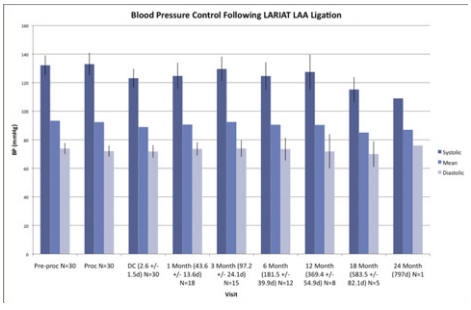
Introduction: The left atrial appendage (LAA) contributes to sodium balance and blood pressure (BP) regulation via

secretion of atrial natriuretic peptide (ANP) granules. Studies have suggested a BP-lowering effect may be seen acutely after LAA excision or ligation. We sought to define the long-term hemodynamic effect of LAA ligation via the LARIAT ligature.
Methods: All patients undergoing LAA ligation via LARIAT were enrolled in a prospective registry. Demographics and clinical history were recorded, as were BP and relevant medications at the pre-procedure visit, on the day of procedure, discharge, and at routine followup. LAA ligation was performed under general endotracheal anesthesia, via standard transseptal and subxiphoid approach.
Results: 30 patients underwent LARIAT LAA ligation, followed for 204 patient-months. 47% were male. CHADS2-VASC score was 4.8 +/- 1.4. HAS-BLED score was 3.9 +/- 1.1. All had a history of hypertension, on at least one anti-hypertensive; 72% were on a diuretic. After LAA ligation, a significant reduction was seen in systolic BP at discharge (123 +/- 18mmHg) compared to pre-procedure (132 +/- 19mmHg) with no significant post-op pericardial effusions. At long-term followup, there was a trend toward lower SBP which was not statistically significant. There was no difference in diastolic BP, or the number or dosing of antihypertensive agents following LARIAT LAA ligation.
Conclusions: LAA ligation is associated with a decrease in systolic BP, but the effect is short-lived. Early release of ANP with LAA ischemia is likely compensated by other homeostatic mechanisms. There is no long-term adverse hypertensive effect of LAA ligation.

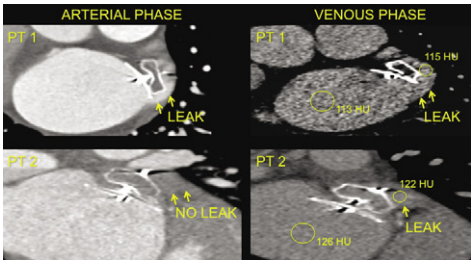


AB13-03

PREVALENCE AND CHARACTERISTICS OF PERI-DEVICE LEAKS ON MULTIDETECTOR COMPUTED TOMOGRAPHY AFTER LEFT ATRIAL APPENDAGE CLOSURE

Claudia Camaioni, MD, Xavier Iriart, MD, Olivier Corneloup, MD, Zakaria Jalal, MD, Hubert Cochet, MD, PhD and Jean-Benoit Thambo, MD. Hopital Haut Lévèque, Pessac, France, C.H.U de Bordeaux, Pessac, France, CHU Bordeaux - Université de Bordeaux, Pessac, France, Hôpital Du Haut - Leveque, Cardiology, Pessac, France

Introduction: The non-invasive detection of peri-device leaks after catheter-based left atrial appendage (LAA) occlusion remains challenging on TEE. The precise prevalence of leaks is thus largely unknown. We assessed the prevalence and characteristics of peri-device leaks after LAA occlusion with the use of CT.
Methods: Cardiac-gated CT using a dual-phase protocol (arterial and venous) was performed in consecutive patients with non-valvular AF 24h before and 3 months after LAA closure with Amplatzer Cardiac Plug (ACP) or WATCHMANN devices. Peri-device leaks were defined as a persisting enhancement of the LAA by the contrast agent. The neck of all leaks was measured (maximum dimension) and its location characterized. Baseline characteristics, including CT data, were analyzed to look for potential predictors of peri-device leaks.
Results: 63 patients were included (age 72±9 yrs, 23 women, CHADS2VaSC2 4.6±1.6, HASBLED 3.8±1.0). Compared to mean landing zone diameter on CT devices were oversized by 2.8±1.9 mm (1.13±0.13 ratio). Follow-up CT detected peri-device leaks in 41 (65%) patients. Maximum leak neck dimension was 4.1±2.4mm. The most common leak location was posterior (66% vs inferior 25%, superior 17%, anterior 6%, P<.001). No clinical or device related factor was found predictive of peri-device leaks, but small landing zones on pre-procedural CT showed a trend towards less leaks (P=0.06).
Conclusions: Peri-device leaks are detected on dual-phase cardiac CT in the majority of patients 3 months after catheter-based LAA occlusion, the most common location being posterior. Prognostic implications should be addressed in future studies.



AB13-04

ACUTE AND LONGTERM OUTCOMES OF PERCUTANEOUS LEFT ATRIAL APPENDAGE SUTURE LIGATION: RESULTS FROM A UNITED STATES MULTICENTER EVALUATION

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Introduction: The limited data regarding epicardial ligation of left atrial appendage (LAA) has discordant results regarding the safety.
Objectives: To delineate the safety and efficacy of LAA closure with the LARIAT device for LAA ligation.
Methods: This is a retrospective, multicenter registry of 750 consecutive patients (mean age 71.9±10 years) undergoing attempted LAA ligation with LARIAT device at 18 hospitals in United States. The primary endpoint was procedural success, defined as successful suture deployment and no leak by intra-procedure transesophageal echocardiography (TEE), and no major complication at discharge (death, stroke, cardiac

perforation requiring cardiac surgery major or bleeding requiring transfusion). A leak of 2-5 mm on follow up TEE was the secondary endpoint.
Results: The LARIAT was successfully deployed in 720 (96 %) patients. Out of these patients, the complete closure was achieved in 707 (98.2%) patients. Thirteen patients (1.8%) had a trace leak (2 weeks of treatment with NSAIDs/Colchicine, pericardial and pleural effusion after discharge) occurred. Peri-procedural use of colchicine reduced the cumulative incidence of delayed complications (8.4% versus 1.58 %, p <0.0001). The follow up TEE was available in 480 patients and showed a leak of 2-5 mm in 6.5 % (31/480) and a thrombus in 2.5 % (12/480). One patient had a leak of > 5 mm.
Conclusions: This largest multicenter experience shows that ligation of LAA with epicardial approach effectively closes the LAA; and has acceptable procedural risks with the evolution of the use of the MP needle for pericardial access and colchicine to mitigate the post-inflammatory response associated with LAA ligation and pericardial access.

AB13-05

CHARACTERISTICS OF THE OPEN SMOOTH VESTIBULE OF THE LEFT ATRIAL APPENDAGE AND ITS ROLE IN THROMBUS FORMATION IN PATIENTS WITH ATRIAL FIBRILLATION AND SURGICAL APPENDAGE CLIP IN SITU

Yalçın Gökoğlan, MD, Sanghamitra Mohanty, MD, FHRS, Carola Gianni, MD, Chintan Trivedi, MD, Rong Bai, MD, J. David Burkhardt, MD, Javier E. Sanchez, MD, Patrick Hranitzky, MD, FHRS, G. Joseph Gallinghouse, MD, Amin Al-Ahmad, MD, FHRS, Rodney P. Horton, MD, Luigi Di Biase, MD, PhD and Andrea Natale, MD, FHRS. Texas Cardiac Arrhythmia Institute, Austin, TX

Introduction: Atrial fibrillation (AF) is a significant risk factor for embolic stroke originating from the left atrial appendage (LAA). LAA occlusion is recommended in patients that are not amenable to anticoagulation therapy because of elevated CHADS2 or CHA2DS2-VASC score. We assessed the risk of stroke off anticoagulants in AF patients following LAA occlusion with appendage clip device.
Methods: One hundred eighty-five AF patients (age 66±13, males 69%, CHADS2 2.6± 0.8, CHA2DS2-VASC 3.5± 1.2) that received surgical left atrial appendage occlusion device (clip) were included in this analysis. Transesophageal echocardiogram (TEE) was performed at the end of the procedure to evaluate successful closure of the vestibule of the LAA and was repeated at 1 and 6-month post-procedure. Patients remained on oral anticoagulants for 1-month post-procedure after which it was discontinued. All patients were monitored for thrombo-embolic complications for at least 1 year by TEE, clinic visits at 3-month intervals and phone calls by our research staffs.
Results: The follow-up TEE revealed the LAA clip to be stable without any secondary displacement. No LAA thrombus was detected. Interestingly, in 177 (95.6%) patients, TEE revealed the proximal part of the smooth vestibule of the LAA neck below the clip, to be still open. This pouch measured 0.8±0.19 cm in depth. At the end of the 24±3 months of follow-up, no stroke or transient ischemic attack (TIA) or other neurological events were observed in the study population (0 of 155, 0%).
Conclusions: In patients with AF in whom oral anticoagulation is deemed unsuitable because of high CHADS2 or CHA2DS2-VASC score, left atrial appendage closure with surgical clip device seems to be safe and effective in preventing stroke. It is relatively common to find incomplete obliteration of the LAA with the surgical clip with the proximal portion of the smooth vestibule still remaining open. However, presence of the open smooth-vestibule with a depth of < 1cm did not increase the risk of stroke even after discontinuation of anticoagulants at the short-term follow-up.

ABSTRACT AB14:
Correlation of Anatomy and Mapping Data for Ventricular Arrhythmia Management

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB14-01

ANATOMICAL PITFALL IN 3D MAPPING, RIGHT VENTRICULAR RECESS (UNEXPECTED STRUCTURE IN FREE WALL OF RIGHT VENTRICULAR OUTFLOW TRACT)

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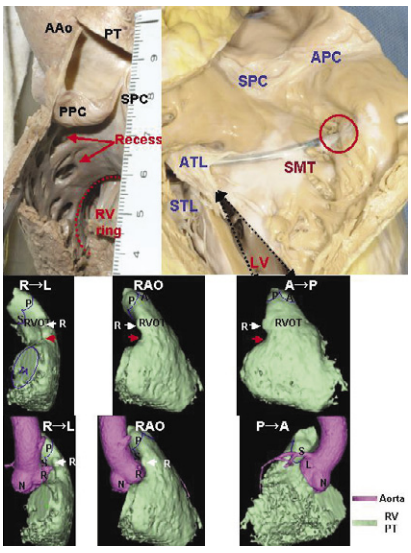
Introduction: The aim of this study was to investigate structural characteristics in free wall (FW) of right ventricular outflow tract (RVOT) and to study the pitfall in doing catheter ablation or 3D mapping anatomically.
Methods: RVOTFW was investigated macroscopically and histologically in 120 autopsied hearts (73males, 78+/-9y.o.) without cardiac diseases.
Results: As shown in figure, there was deep and large recess in RVOTFW (see arrows) just below posterior pulmonary cusp. Its endocardial surface revealed relatively smooth, and its wall thickness was very small. These findings could be found in all studied hearts.
Conclusions: We should take deep, large and thin-walled recess with smooth surface in RVOTFW into consideration to avoid complications associated with catheter ablation.



AB14-02

VOLTAGE THRESHOLD FOR HIGH DENSITY MAPPING CATHETER WITH SHORT INTERSPACED SMALL ELECTRODES

Frederic Sacher, MD, PhD, Josselin Duchateau, MD, Stefano Capellino, Eng., Benjamin Berte, MD, PhD, Nicolas Derval, MD, Arnaud Denis, MD, Sana Amraoui, MD, Arnaud Chaumeil, MD, Gregoire Massoullie, MD, Meleze Hocini, MD, Michel Haissaguerre, MD and Pierre Jais, MD. LIRYC Institute / Hôpital Cardiologique Haut-Lévêque, Bordeaux, France, Boston Scientific, Bordeaux, France, Hopital Cardiologique du Haut Leveque, Bordeaux, France, Hopital du Haut Leveque, Pessac, France, CHU Bordeaux, Bordeaux, France, Hopital Haut Leveque, Pessac, France, Hôpital Haut-Lévêque, Bordeaux, France, LIRYC Institute, University Hospital of Haut Lévèque, Bordeaux-Pessac, France, Hopital Cardiologique Haut Leveque - Université Bordeaux, Pessac, France, CHU Bordeaux - Bordeaux University, Bordeaux, France

Introduction: Since the seminal work of Marchlinski et al. in 2000 with ablation catheters, it has been widely accepted that thresholds for border zone (BZ) and dense scar on 3D electroanatomic mapping system have to be set at 1.5 and 0.5 mV. Since then, several dedicated mapping catheter with short interspaced, small electrodes have been developed and used for substrate mapping however the same thresholds have been applied without further investigations. Our aim was to find voltage thresholds that identify accurately the scar and BZ area when mapping with a dedicated catheter (ORION, Boston Scientific)
Methods: Voltage maps were acquired with an Orion catheter (Rythmia, Boston Scientific) in 4 sheep with chronic myocardial infarction. In vivo high resolution cardiac MRI before the procedure and 9.4 Tesla MRI on explanted heart were performed after to assess the true dense scar and border zone areas. Data from MRI and Rythmia were exported into Mathlab to identify the better sensibility and specificity of voltage threshold to identify scar based on MRI. In the second part of the study, all patients with high resolution cardiac MRI referred for VT ablation performed with the Rythmia system were analyzed to test the threshold defined earlier. Voltage maps were exported and compared with MRI delayed enhancement maps. Percentage of overlap between dense scar/BZ on MRI and on voltage map using the defined threshold was analyzed.
Results: In sheep, a mean of 14389 ±4467 points were acquired per LV map. The optimal voltage threshold to identify dense scar based on both in vivo MRI and 9.4T MRI was <0.1mV. The voltage identifying best the limit between BZ and normal myocardium was in average 1 mV but varied from 0.5 mV to 1 mV depending on animals. Five patients (4 M, 66 ±9yo) with ischemic cardiomyopathy were included in the human part of the study. A total of 11345 ±3257 points were acquired for the SR voltage map. Using a 0.1-1 mV threshold, percentage of overlap of dense scar/ BZ of voltage map vs MRI were respectively 89 ±19 % and 76 ±32%.
Conclusions: Thresholds to define dense scar and border zone on voltage map may differ according to the catheter used depending on its electrodes size and distance. Concerning the Orion catheter (Boston Scientific), the optimal threshold for voltage map appears to be 0.1-1mV.

AB14-03

DEFINING A NEW CUT-OFF VALUE FOR UNIPOLAR VOLTAGE IN THE RIGHT VENTRICLE TO DETECT EPICARDIAL SCAR USING CT DERIVED FAT INTEGRATION

Jeroen Venlet, MD, Gijsbert FL. Kapel, MD, Sebastiaan R. Piers, MD, Marta de Riva Silva, MD, Rob Van der Geest, Eng. and Katja Zeppenfeld, MD, PhD. Leiden University Medical Center, Leiden, Netherlands

Introduction: Unipolar endocardial voltage (UEV) at sites with normal bipolar endocardial voltage (BEV) may accurately detect epicardial scar. Currently applied UEV cut-off values for epicardial scar are based on studies that did not correct for the highly variable epicardial fat layer attenuating BV.
Methods: Consecutive patient who underwent combined endo/epicardial RV electroanatomical mapping (EAM) with integration of CT-derived fat mesh between 2006 and 2015 were included. Epicardial and pericardial contours were semi-automatically traced on short axis views for fat thickness (FT). After EAM epicardial points were exported and superimposed on the corresponding short-axis CT slice to evaluate local FT. 3D coordinates of each point were exported to Matlab and endocardial and epicardial points were linked based on shortest distance. For analysis point pairs with BEV >1.5mV and ≤1mm FT were selected. Receiver operating characteristics curve analysis was performed to determine the optimal cut-off value, for endocardial UV to detect epicardial low BV.
Results: Of the 30 pts included (50±15 years, 77% male 23, BMI 25±4 kg/m2), 15 had definite ARVC, 13/15 a pathogenic mutation, 2 borderline ARVC , 3 cardiac sarcoidosis, 1 scar of unknown origin, 8 athlete's RVOT scar, and 1 myocarditis. The median FT was 2.9 mm (IQR 1.6 - 5.3 mm). A total of 6750 endocardial points was coupled to the closest epicardial points and 3997 (60%) point pairs had a distance <10mm when corrected for FT. Of these, a total of 351 (5%) point pairs were selected (BEV >1.5mm, FT≤1mm). For endocardial UV, the optimal cut-off value to detect areas with epicardial BV<1.5mV was 3.92mV (AUC 0.73; sensitivity 0.58, specificity 0.79).This cut-off was more specific for epicardial scar than the previously proposed 4.4mV and 5.5mV (specificity 0.72 and 0.54, respectively).
Conclusions: This is the first study to propose an endocardial UV cut off of 3.92mV to detect epicardial scar using CT image integration to correct for epicardial fat thickness. Prior proposed cut-off values overestimate the epicardial scar.

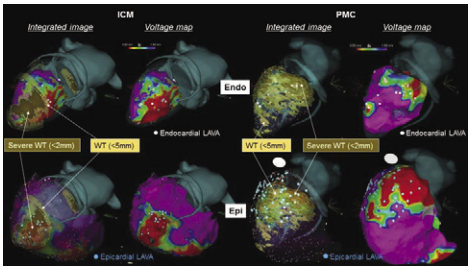
AB14-05

MYOCARDIAL WALL THINNING ON MDCT RELATES TO THE TRANSMURAL DISTRIBUTION OF ABNORMAL VENTRICULAR ACTIVITIES DURING SINUS RHYTHM IN PATIENTS WITH SCAR-RELATED VENTRICULAR TACHYCARDIA OF VARIOUS ETIOLOGIES

Seigo Yamashita, MD, PhD, Frédéric Sacher, MD, PhD, Darren Hooks, MD, PhD, Benjamin Berte, MD, PhD, Jean-Marc Sellal, MD, Antonio Frontera, MD, Nora Al. Jefairi, MD, Yuki Komatsu, MD, Sana Amraoui, MD, Arnaud Denis, MD, Nicolas Derval, MD, François Laurent, MD, Michel Montaudon, MD, PhD, Mélèze Hocini, MD, Michel Haïssaguerre, MD, Pierre Jaïs, MD, PhD and Hubert Cochet, MD, PhD. Hôpital Cardiologique du Haut Lévèque, Pessac, France, Univ of Auckland School of Medicine, Auckland, New Zealand

Introduction: Scar-related VT arises from specific substrate according to etiology. We assessed the relationship between wall thinning (WT) on computed tomography (CT) and the endo vs epicardial distribution of local abnormal ventricular activity (LAVA) in ischemic cardiomyopathy (ICM), post-myocarditis (PMC) and dilated cardiomyopathy (DCM).
Methods: 42pts (58±13y, 22 ICM, 11 PMC, 9 DCM) underwent CT before a combined endo/epicardial VT ablation. WT (<5mm) and severe WT (SWT) (<2mm) on CT were registered to sinus rhythm voltage and LAVA maps. We assessed the endo vs epicardial distribution of LAVA according to WT. Endo/epicardial facing LAVA were defined as distinct potentials recorded less

than 3mm from each other on opposite sides of the wall.
Results: WT/SWT were found in 36(86%)/20(48%) pts with areas of 42±37/26±24cm2. SWT was frequently detected in ICM (77% vs. PMC 27% and DCM 0%, P<0.001). Endocardial LAVA were more likely found in ICM (27[15-40] points/map vs. PMC 0[0-6] and DCM 4[0-18], P<0.001) and epicardial LAVA in PMC (55[43-83] points/map vs. ICM 19[12-41] and DCM 24[0-45], P=0.005). Endo/epicardial facing LAVA were frequently found within SWT area (91% in 5mm, P<0.001). In SWT areas, the presence of endocardial LAVA in ICM and epicardial LAVA in PMC predicted opposite facing LAVA with 78/48% and 79/98% of sensitivity/specificity. SWT predicted epicardial LAVA in ICM and endocardial LAVA in PMC with 89/100% and 100/100% sensitivity/specificity.
Conclusions: SWT is frequently found in ICM and PMC, and not common in DCM. The endo/epicardial distribution of LAVA depends on the etiology, but SWT predicts LAVA on opposite side of the wall (epicardial in ICM and endocardial in PMC).

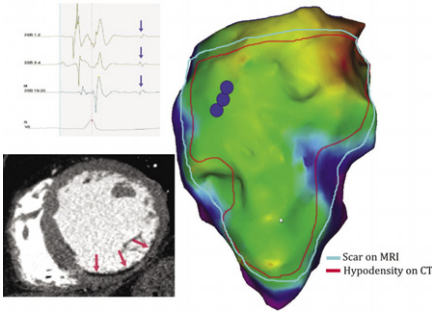


AB14-06

FAT DEPOSITION WITHIN MYOCARDIAL INFARCTION: CLINICAL AND ELECTROPHYSIOLOGICAL CORRELATES IN PATIENTS WITH POST-INFARCTION VENTRICULAR TACHYCARDIA

Ghassen Cheniti, MD, Elvis Teijeira-Fernandez, MD, Masateru Takigawa, MD, Frederic Sacher, MD, Arnaud Chaumeil, MD, Antonio Frontera, MD, Seigo Yamashita, MD, Jean-Marc Sellal, MD, Nathaniel Thompson, MD, Nora Eljefairi, MD, Jean_Yves Wielandts, MD, Claudia Camaioni, MD, Sana Amraoui, MD, Arnaud Denis, MD, Gregoire Massoullie, MD, Nicolas Derval, MD, Meleze Hocini, MD, Michel Haissaguerre, MD, Pierre Jais, MD and Hubert Cochet, MD. Hopital Cardiologique du Haut Lévêque, Pessac Bordeaux, France

Introduction: Fat deposition is frequently observed in chronic ventricular infarction. We studied clinical and electrophysiological correlates of fat deposition in patients with ischemic VT.
Methods: 63 consecutive patients (age 66±12 yrs, 4 women) with ischemic VT underwent contrast-enhanced MDCT. Myocardial fat deposition was identified as areas of pixel density < -10 HU, and related to clinical characteristics. Its relationship with electrophysiological VT substrate was analyzed in a subset of 26 patients undergoing endocardial sinus rhythm mapping.
Results: Fat was found on MDCT in 41/ 63 MI scars (65%). Fat did not relate to clinical characteristics (age, gender, risk factors, vascular territory, revascularization method, ventricular function or medical therapy) except for delay since infarction, fatty scars being older (18±12 vs 12±9 yrs, P=.05). In the population undergoing contact mapping, a total of 1847 electrograms within scar were analyzed (1336 in scars with fat and 511 in those without). The presence of fat did not relate to scar size (P=.21), but to lower bipolar voltage (0.6 mV [Q1-Q3 0.3-1.2] vs 0.8 mV [Q1-Q3 0.4-1.6]; P<.001). The rate of local abnormal ventricular activity (LAVA) did not differ between scars with and without fat (49% vs 55% of points within scar, P=.26), but LAVA in fatty scars showed a longer delay after QRS onset (109 ± 53 vs 96±32 ms; P=.004) and a lower bipolar amplitude (0.16 mV [Q1-Q3 0.1-0.25] vs. 0.23 mV [Q1-Q3 0.14-0.36]; P<.001).
Conclusions: Fat deposition is found in 2/3 patients with ischemic VT and correlates with scar age. These scars show lower bipolar voltage and more delayed LAVA.



ABSTRACT AB15:
Atrial Fibrillation: Risk Factors and Mechanisms

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB15-01

THE RISK OF ATRIAL FIBRILLATION AFTER BARIATRIC SURGERY IN PATIENTS WITH MORBID OBESITY WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA

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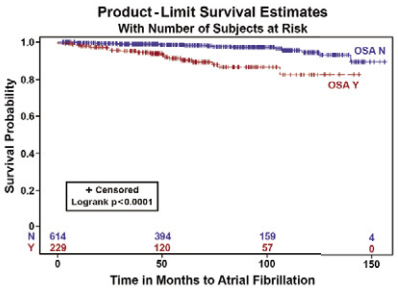
Introduction: Weight loss after bariatric surgery in morbidly obese patients reduces atrial fibrillation (AF); however, it is not known if similar benefits are maintained in patients with and without obstructive sleep apnea (OSA). We sought to determine whether weight loss after laparoscopic adjustable gastric banding (LAGB) had a similar effect on new onset AF event rates in patients with and without OSA.
Methods: Differences in LAGB-induced weight loss on incident AF in those with OSA and matched non-OSA patients were determined by Kaplan-Meier and Cox regression analysis and predictors of AF after LAGB identified.
Results: Out of 843 morbidly obese patients [body mass index (BMI) ≥35 kg/m2] who underwent LAGB (mean age 44±11 years, mean BMI 49±8 kg/m2) and were followed for 11 years, new onset AF was documented in 38 (4.5%). The mean reduction in

BMI over the median follow-up of 63.6 months was 11 kg/m2. Despite similar weight loss, patients with OSA had significantly higher rate of incident AF compared to those without OSA (Figure; at 5 years 9.8% vs 1.8%, p<0.0001). On multivariate analysis, OSA (HR=2.3; 95% CI 1.1- 4.7, p<0.01) and age (HR 1.19 for every 10-year; CI 1.0-1.16, p<0.0001) were independent predictors of new onset AF, while gender, race, baseline BMI, hypertension and diabetes were not.
Conclusions: Patients with OSA, despite a similar weight loss to those without OSA after LAGB, had a significantly higher rate of AF events. Further investigation is warranted into whether compliance with OSA treatment helps reduce AF events.



AB15-02

HIGHEST DOMINANT FREQUENCY AND ROTOR POSITIONS ARE STABLE MARKERS FOR ATRIAL DRIVER LOCATION IN NON-INVASIVE MAPPING OF ATRIAL FIBRILLATION: A COMPUTATIONAL STUDY

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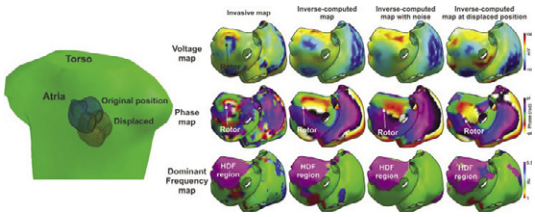
Introduction: Inverse-computed Dominant Frequency (DF) and rotor maps have been proposed as non-invasive mapping techniques to locate atrial drivers maintaining atrial fibrillation (AF). This study evaluates the stability of both techniques to identify atrial drivers under the effect of electrical noise or spatial uncertainties.
Methods: Inverse-computed DF and phase maps were obtained on a population of 31 different mathematical simulations of AF maintained by a single rotor. Highest DF (HDF) regions and rotor position were compared with the same measurements from non-invasive mapping after addition of white noise to the ECG (90-0 dB signal-to-noise ratio) and with linear (0-5 cm) and angular deviations (0-45º) in the atrial position.
Results: Inverse-computed EGMs showed individually a poor correlation with the actual EGMs even under the best conditions (correlation coefficient 0.45±0.12) and worsened with the artifacts to 0.22±0.11 with 10 dB noise, 0.01±0.02 with 3 cm displacement and 0.02±0.03 with 36º angular deviation. However, inverse-computed HDF regions showed stability against artifacts: from 82±18% match for the HDF region for the best conditions, down to 73±23% for 10 dB of noise, 77±21% for 5 cm displacement and 60±22% for 36º angular deviation. The rotor position also presented a stable measurement: the distance from the inverse-computed rotor to the actual rotor was 2.2±3.5 cm for the best conditions, 3.6±4.7 cm for 10 dB of noise, 4.2±3.2 cm for 4 cm displacement and 3.3±1.5 cm for 36º.
Conclusions: Identification of atrial sources based on HDF and rotor location from non-invasive mapping is accurate even in the presence of noise and uncertainty in the atrial location.



AB15-03

RELATIONSHIP BETWEEN FOCAL SITES MAINTAINING PERSISTENT ATRIAL FIBRILLATION AND ATRIAL FIBROSIS IN PATIENTS - STUDIES USING HIGH DENSITY (510-512 ELECTRODES) BI-ATRIAL EPICARDIAL MAPPING

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Introduction: Recently, we demonstrated that in patients with persistent atrial fibrillation (PerAF), activation from multiple foci (sustained and/or intermittent) of different cycle lengths (CLs) maintains AF. Low voltage and less fractionated electrograms are electrical markers of fibrosis. The aim of this study was to evaluate the relationship between foci (sustained and intermittent) and electrical markers of fibrosis during high density mapping of AF in patients with PerAF.
Methods: We recorded the sequence of atrial activation during 11 episodes of AF in 11 patients with PerAF (1 month - 9 yrs) at open heart surgery. During AF, atrial electrograms (AEGs) were simultaneously recorded from both atria for 1 - 5 minutes from 510-512 epicardial electrodes, along with ECG lead II. From each patient, 32 consecutive secs of AEG analysis that identified sustained and/or intermittent foci was performed. These focal sites were assessed for fractionation by criteria for complex atrial fractionated electrogram (CAFÉ) (< 120 ms). AEG voltage (peak-to-peak) was measured at all sites.
Results: During PerAF, 8 sustained foci (mean CL 170±19 ms; range 142-200 ms; duration 32 s) and 21 intermittent foci (mean CL 176±18 ms; range 143-211 ms) were identified in all patients. The voltages of 6/8 sustained and 13/21 intermittent foci were less than mean voltage of both atria. The voltages of sustained foci (mean 0.72 mV, median 0.23 mV) were lower than the intermittent foci (mean 1.88 mV, median 0.95 mV) ($p < 0.05$). Both sustained and intermittent focal sites were less fractionated by CAFÉ criteria (sustained foci 0/8; intermittent foci 2/21).
Conclusions: During PerAF, sustained and intermittent foci demonstrated electrical makers of fibrosis characterized by lower voltages and less fractionation. However, sustained focal sites had lower voltages and less CFAÉ (more atrial fibrosis) than intermittent foci.

AB15-04

ASYNCHRONOUS EXCITATION OF THE RIGHT ATRIAL WALL DURING ATRIAL FIBRILLATION IN HUMANS

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Introduction: There is much controversy about the mechanisms underlying perpetuation of atrial fibrillation. Until now, the hypothesis of transmural asynchrony enabling creation of new fibrillation waves on the opposite side was never demonstrated in humans. The aim of this study is to demonstrate the occurrence of asynchronous endo-epicardial excitation of the atrial wall during atrial fibrillation.
Methods: During cardiac surgery, simultaneous endo- and epicardial mapping was performed with two 128-electrode arrays positioned precisely opposite to each other, like a pair of thongs. The array for endocardial mapping was inserted through the incision for venous cannulation in the right atrial appendage. From 14 patients (10 with and 4 without atrial fibrillation), recordings of 10 seconds of (induced) atrial fibrillation were analyzed to determine the incidence of asynchronous excitation times (≥15ms) of opposite endo- and epicardial electrodes.
Results: The degree of endo-epicardial asynchrony ranged between 0.9-55.9% in the study population with a standard deviation of excitation time differences ranging from 4.2 to 37.2 ms. The asynchronous excitation demonstrated a high degree of spatio-temporal variation without preference for either side. Focal waves appeared equally frequent at endocardium and epicardium (579 vs 620). Using strict criteria for breakthrough (presence of an opposite wave within 4mm and ≤14ms before the origin of the focal wave), the majority (65%) of all focal fibrillation waves could be attributed to transmurally conducting fibrillation waves.
Conclusions: This study is the first to demonstrate the occurrence of asynchronous excitation of the right atrial wall during human atrial fibrillation, supporting the hypothesis of transmural conduction of fibrillation waves. Endo-epicardial asynchrony may, therefore, stabilize the process of atrial fibrillation and explain the failure of ablative therapy in some patients with atrial fibrillation.

AB15-05

TISSUE WAVELENGTH ESTIMATION IN HUMAN ATRIAL FIBRILLATION. CORRELATION WITH PULMONARY VEIN ANTRAL SIZE

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Introduction: In persistent atrial fibrillation (AF), spectral Frequency which accelerates after adenosine, suggests reentrant mechanism. In functional reentry the circuit length would be determined by and equal to tissue wavelength. Determining the circuit length would give a better insight into potential location sites of reentry.
Methods: In 12 AF patients, refractory period studies (A1-A2) to induce AF were done. Using a multi spline catheter with 10 bipolar electrodes and assuming centrifugal spread from the stimulating electrode, conduction velocity (CV) was measured in the mapped area both during A1-A1 and A1-A2. Once induced, an area of organized activity was mapped the cycle length (CL) was measured, before and after 12 mg of adenosine (Ado). Circuit length was calculated CV × CL. Pulmonary vein antral (PVA) diameter and intra atrial distances were measured using CT images and 3D mapping system.
Results: The CL of organized atrial activation decreased from 223±38 to 181±43 ms ($p<0.05$). The mean CV during A1-A2 was 0.24±.08 m/s and during A1-A1 0.43±0.05 m/s. The calculated tissue wavelength or circuit length (CV×CL) was in range of 53.4mm and 95.89 mm depending on CV value used. The circuit shortened post Ado to 43.44 mm and 77 mm respectively. The PVA diameter in this group was 77.05±7mm 49.5-102.2mm). The distance to contralateral PVA was 63.1±13.1mm.
Conclusions: The calculated tissue wavelengths (or circuit lengths in functional reentry) are in the range of PVA diameters even when CL shortens, as expected, post adenosine or CV changes. This raises the possibility of PVA as suitable potential location of reentrant circuits in human AF.

AB15-06

ALCOHOL CONSUMPTION, LEFT ATRIAL DIAMETER, AND ATRIAL FIBRILLATION

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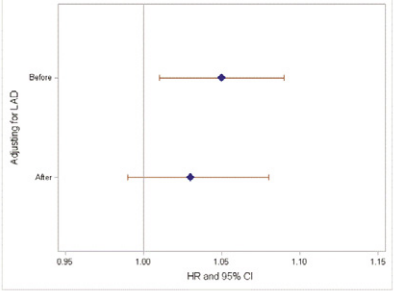
Introduction: Alcohol consumption has been associated with atrial fibrillation (AF) in several epidemiologic studies, but mechanisms remain unknown. We sought to test the hypothesis that an atrial myopathy, manifested by echocardiographic left atrial enlargement, explains the association between chronic alcohol use and AF.
Methods: We evaluated the relationship between cumulative alcohol consumption and risk for AF in 4,888 Offspring and Original Framingham Heart Study participants (mean age 58.9 years, 55% women) with left atrial size measurements per echocardiography and free of prevalent AF at the first echocardiographic measurement.
Results: The overall incidence of AF was 8.7 per 1000 person years (685 incident AF cases developed out of 13,223 observations and over a median 4.5-year follow-up [25th -75th percentiles 3.8 to 8.5 years]). After multivariable adjustment, every additional 10 g of alcohol per day (just under 1 drink per day) was associated with a 0.18 mm (95% CI 0.10-0.26 mm) larger left atrial dimension. In multivariable adjusted prospective analysis, every 10 g per day of alcohol consumed was associated with a 5% higher risk of developing new-onset AF (Hazard Ratio [HR] 1.05, 95% CI 1.01-1.09). An estimated 30% of the association between alcohol and AF risk was explained by left atrial enlargement (Figure 1).
Conclusions: Our study of a large, community-based sample identified alcohol consumption as a predictor of left atrial enlargement and subsequent incident AF. Left atrial enlargement may be an intermediate phenotype along the causal pathway linking long-term alcohol consumption to AF.

Figure 1. Forest plot showing change in hazard ratio (HR) between alcohol and atrial fibrillation before and after adjustment for left atrial dimension (LAD).



ABSTRACT AB16:
CRT: Lessons Learned from EKG Patterns and Parameters

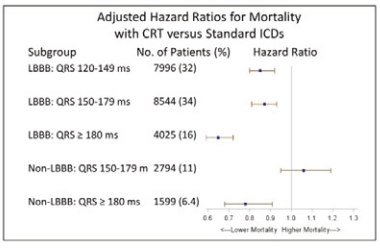
Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB16-01

OUTCOMES WITH CARDIAC RESYNCHRONIZATION THERAPY AND STANDARD IMPLANTABLE CARDIOVERTER DEFIBRILLATORS IN PATIENTS WITH A VERY WIDE QRS DURATION (QRS > 180 MS): A MEDICARE ICD REGISTRY ANALYSIS WITH PROPENSITY MATCHING

Varun Sundaram, MD, Jayakumar Sahadevan, MD, Albert L. Waldo, MD, PHD, FHRS, Yogesh NV. Reddy, MD, Samuel J. Asirvatham, MD, FHRS, Judith A. Mackall, MD, Anselma Intini, MD, Brigid Wilson, PhD, Daniel I. Simon, MD and Kenneth C. Bilchick, MD, FHRS. University Hospitals Case Medical Center, Cleveland, OH, Case Western Reserve Univ, Univ Hospital of Cleveland, Beachwood, OH, Case Western Reserve University - University Hospitals Case Medical Center, Cleveland, OH, Mayo Clinic, Rochester, MN, University Hospitals, Case Medical Center, Cardiology, Cleveland, OH, Veteran Affairs Medical Center, Cleveland, OH, University of Virginia Health System, Charlottesville, VA

Introduction: Outcomes with cardiac resynchronization therapy defibrillators (CRT-D) in patients with a very wide QRS duration ≥180ms are not well established because these patients have been under-represented in clinical trials.
Methods: Medicare patients from the ICD Registry with CRT-D and a confirmed current class I or IIa indication for CRT-D were matched using propensity methods to patients with a standard ICD who also had a class I or IIa indication for CRT-D but did not receive CRT-D. Adjusted hazard ratios for mortality over 4 years with CRT-D versus standard ICDs based on QRS duration and morphology were determined with Cox proportional hazards regression.
Results: The 24,958 patients (age 73.0±10.5 years, 28.5% female, 50.2% with prior myocardial infarction, and 17.6% with non-LBBB) were composed of 12,478 with CRT-D matched to 12,480 with standard ICDs. All patients with LBBB had improved 4-year survival with CRT-D versus standard ICDs regardless of QRS duration, but those with QRSD>180ms had the greatest adjusted survival benefit (HR 0.649 [95%CI 0.588-0.716]). Among patients with non-LBBB, although overall CRT-D survival rates were lower compared with LBBB, there was a survival benefit with CRT-D versus matched standard ICD patients at 4 years in the subgroup with QRSD>180ms (adjusted HR 0.784 [95%CI 0.676-0.909]), but not in those with QRSD 150-179 ms (Figure).
Conclusions: Although CRT-D is presently indicated for non-LBBB with QRSD ≥ 150 ms, CRT-D did not confer a survival benefit in patients with non-LBBB and QRS 150-179 ms, but was associated with improved survival with non-LBBB and QRSD ≥ 180 ms. This has implications for guideline indications for CRT-D in non-LBBB.



AB16-02

THE ASSOCIATION BETWEEN A PROLONGED PR INTERVAL AND OUTCOMES OF CARDIAC RESYNCHRONIZATION THERAPY: A REPORT FROM THE NATIONAL CARDIOVASCULAR DATA REGISTRY

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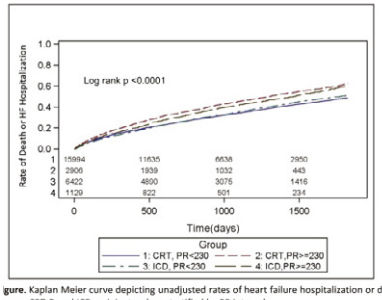
Introduction: A prolonged PR interval is common among cardiac resynchronization therapy (CRT) candidates; however, the association between PR interval and outcomes is unclear and data are conflicting.
Methods: We conducted inverse probability weighted (IPW) analyses of 26,451 CRT eligible (EF ≤35, QRS ≥ 120ms) patients from the National Cardiovascular Data Registry Implantable Cardioverter Defibrillator (ICD) Registry to determine the association between prolonged PR interval (≥230ms), receipt of CRT with ICD (CRT-D) vs ICD, and outcomes. Patients were followed up to 5 years for incident heart failure hospitalization (HFH) or death as defined by Medicare claims. Subgroup analyses were performed using IPW models for each subgroup.
Results: Patients with a PR≥230ms (15%;n=4,035) were older and had more comorbidities including coronary disease, atrial arrhythmias, diabetes, and kidney disease. After propensity matching and risk-adjustment, PR≥230ms was associated with increased risk of HFH or death among CRT-D (HR 1.23, CI 1.14-1.31, p<0.001) but not ICD recipients (HR 1.08, CI 0.97-1.20, p=0.17) (pinteraction= 0.043). CRT-D (vs. ICD) was associated with lower rates of HFH or death among patients with PR<230ms (HR 0.79, CI 0.73-0.85, p<0.001) but not PR≥230ms (HR 1.01, CI 0.87-1.17, p=0.90) (pinteraction = 0.0025)(Figure);this effect was consistent among LBBB and non-LBBB subgroups.
Conclusions: A PR≥230ms is associated with increased rates of HFH or death among CRT-D patients. The comparative effectiveness of CRT-D (vs ICD) is significantly reduced among patients with a PR≥230ms. A better understanding of this relationship is essential.



igure. Kaplan Meier curve depicting unadjusted rates of heart failure hospitalization or death among CRT-D and ICD recipients when stratified by PR interval.

AB16-03

IMPACT OF BASELINE RIGHT VENTRICULAR PACING OR WIDE QRS ON CLINICAL AND ARRHYTHMIC OUTCOMES IN CONTINUOUS FLOW LEFT VENTRICULAR ASSIST DEVICE RECIPIENTS

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Introduction: Prior data from our institution showed no additive benefit for CRT over ICD in the continuous flow (CF) LVAD population but several patients in the ICD arm were RV paced or had a QRS duration >120 msec. In this multicenter study, we sought to assess the clinical and arrhythmic outcomes of CF-LVAD patients with wide QRS or RV pacing at baseline, when compared to narrow QRS or continued CRT-D.
Methods: Analysis was performed in 120 patients with ICD or CRT who underwent CF-LVAD implantation from 2009-2014. Patients were divided into 3 groups: a) ICD group with narrow QRS (ICD-N), b) ICD group with >80% RV pacing or QRS duration >120 msec (ICD-W) and c) CRT-D group. Mortality, all-cause and heart failure (HF) hospitalization, atrial (AA) and ventricular (VA) arrhythmia incidence, and ICD therapies were compared among the 3 groups.
Results: Of 120 LVAD patients (Age 56±14 years, 79% male), 58 had ICD and 62 had CRT-D. In the ICD group, 33 (57%) had >80% RV pacing at baseline/ QRS duration >120 msec. At baseline, no significant differences were noted between the 3 groups in demographics, LVAD type or indication, cardiomyopathy type, comorbid conditions, HF and antiarrhythmic medications, or incidence of VA. AA was significantly lower in the ICD-W group compared to others (23% vs 54%, p=0.01). Mean biventricular pacing in the CRT group was 96%. Mean baseline QRS duration was significantly different between groups (115±44 [ICD-N] vs 137±32 [ICD-W] vs 166±45 msec [CRT-D], P<0.0001). During a mean follow-up of 738±495 days, 21 (34%) died in the CRT group compared to 10 (40%) in the ICD-N group and 5 (15%) in the ICD-W group (p=0.07). Significant improvement in QRS duration occurred in all 3 groups during follow-up but was not associated with improved survival (log rank test, p=0.33). No significant differences were noted between the 3 groups [ICD-N vs ICD-W vs CRT-D] in all-cause, HF hospitalizations, incidence of AA (44% vs 26% vs 38%, p=0.3), VA (37% vs 28% vs 42%, p=0.8), or ICD shocks (24% vs 10% vs 24%, p=ns).
Conclusions: In this large CF-LVAD patient cohort, baseline QRS duration, native or paced, as well as change in QRS duration during follow-up was not significantly associated with improved mortality, hospitalizations or incidence of AA and VA.

AB16-04

DO ALL IVCD ECG PATTERNS RESPOND EQUALLY TO CRT?

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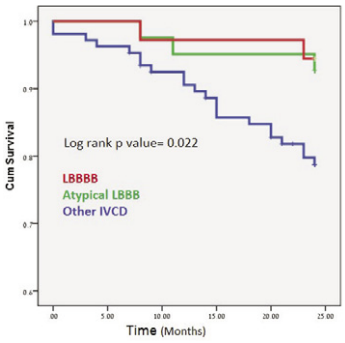
Introduction: Response to cardiac resynchronization therapy (CRT) is well established in patients with typical LBBB pattern, but maybe modest or even negative in the presence of interventricular conduction delay (IVCD). However, IVCD pattern is heterogeneous, and it is possible that patients with IVCD but “atypical LBBB” (ALBBB) pattern may also respond to CRT.
Methods: Consecutive baseline ECGs of 197 patients implanted between 2007-2009 were analyzed. ECGs were classified into 3 groups: A) typical LBBB according to accepted guidelines (n=38); B) IVCD with LBBB pattern in V1 and in 1, AVL but with QS or rS in V5-V6 defined as ALBBB (n=41); C) all other IVCD patterns (n=108). End points were 2 years mortality and clinical response (improvement in a composite score using NYHA functional class, 6-minute walk test, and quality of life questionnaire) at 1-year of follow-up.
Results: Baseline clinical characteristics were similar among all 3 patient groups. Compared to other IVCD, ALBBB was independently associated with a significant increase in the likelihood of clinical (OR=2.9; p=0.01) response at 1 year. Furthermore, clinical response among ALBBB patients was similar to the LBBB group (all p-values> 0.1). Cumulative 2 year survival was 95% in typical LBBB, 90% in ALBBB and 78% in other IVCD patients (p value = 0.022, Figure). The lower mortality risk associated with ALBBB compared with other IVCD persisted after adjustment for age, sex, QRS duration and typical LBBB morphology (HR=0.28; p=0.04).
Conclusions: Not all IVCD patients respond equally to CRT. Those with ALBBB have a favorable response to CRT, including similar survival rates to typical LBBB patients.



AB16-05

CARDIAC RESYNCHRONIZATION DECREASES ABNORMAL CARDIAC SODIUM CHANNEL MRNA SPLICING

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Introduction: Heart failure (HF) downregulates cardiac sodium channel (SCN5A) mRNA and upregulates its mRNA splicing variant D (VD), which encodes a prematurely truncated, nonfunctional channel. Circulating SCN5A variant levels correlate with arrhythmic events in a HF population. Cardiac resynchronization therapy (CRT) improves heart function and decreases arrhythmic events. Hence, we tested whether CRT altered mRNA expression of circulating SCN5A and its VD.
Methods: HF patients with new implantable cardioverter-defibrillators (ICD) for primary prevention were enrolled. Circulating SCN5A and its VD levels at baseline and at a follow-up visit were measured and compared using the ratio of VD to total SCN5A transcripts.
Results: A total of 58 HF patients were enrolled. At enrollment, patients with lower ejection fraction (<30%) had higher circulating VD levels (0.81±0.09 vs 0.75±0.09, P<0.01). There was a significant correlation between VD mRNA expression at enrollment and the presence of CRT (r=0.241, p<0.05), dyslipidemia (r=0.310, p<0.05), valvular heart disease (r=0.275,

p<0.05), chronic kidney disease (r=0.258, p<0.05) and left ventricular end systolic diameter (r=0.347, p<0.05). After a median follow-up of 163 days, the VD ratio had significantly decreased (0.83±0.09 vs 0.72±0.11, P<0.05) in patients receiving CRT-D. In addition, the VD ratio had significantly increased (0.77±0.07 vs 0.84±0.05, P<0.05) in patients receiving single-chamber or dual-chamber ICDs.
Conclusions: HF patients with lower ejection fraction had higher circulating, nonfunctional VD levels. CRT decreased the proportion of nonfunctional sodium channels, which might explain lower arrhythmic risk related to CRT therapy.

AB16-06

RELATION BETWEEN ECG PARAMETERS AND LV ELECTRICAL DELAY IN PATIENTS WITH LEFT VENTRICULAR DYSFUNCTION

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Introduction: The ability to derive left ventricle (LV) electrical delays (Q-LV) from the 12-lead ECG is a critical element to improving application of cardiac resynchronization therapy (CRT). The purpose of this study was to examine the ECG parameters correlated with longer Q-LV.
Methods: one hundred seventy-two patients (130 men, 73±8 y; LV ejection fraction 29 ± 6%) underwent CRT. In according to baseline ventricular conduction delay the patients were categorized in two groups: 1) left bundle branch block (BBB) pattern (QRS d ≥ 130 ms, monophasic QS or rS complex in lead V1/V2 and a RsR complex in lead V6; 2) right (RBBB) pattern (QRS d ≥ 130 ms, dominant terminal R wave in lead V1 with triphasic complex rSR, qR, or R). The following 12-lead baseline ECG parameters were evaluated in LBBB pattern: a) QRS d (> 150 ms), b) mid-QRS notch/slurring in ≥ contiguous lateral leads, c) r wave ≥1 mm in lead V1 and/or a q wave ≥1 mm in lateral lead, d) left QRS axis deviation, e) intrinsicoid deflection (QRS onset to R peak ≥ 60 ms in V6). In patients with RBBB pattern we evaluated: a') QRS d (>150 ms), b') S wave in leads I/aVL, c) left QRS axis deviation. The maximum Q-LV measured into lateral/postero-lateral tributary veins of the coronary sinus were correlated with the above ECG parameters and clinical variables. The frequency of patients with Q-LV>110 ms (cut-off value) was also evaluated in both BBB pattern groups in according to QRS parameters.
Results: In LBBB pattern QRS > 150 ms and mid-QRS notching independently correlated with Q-LV (B=15.3, p<0.0001; B=27.7, p<0.0001 respectively). A Q-LV > 110 ms was observed in all patients (75/75) when both of these ECG parameters were present. In RBBB pattern only S waves in DI/aVL predicted a longer Q-LV value (B= -36.5, p>0.0001). A QLV >110 ms was found in 7/10 patients with a QRS > 150 ms without S wave DI/aVL whereas none patients had QLV >110 ms with typical RBBB (S waves in DI/aVL) despite of QRS > 150 ms. LV end systolic volume correlated with Q-LV only in patients with LBBB pattern.
Conclusions: A longer QRS (>150ms) and mid-QRS notching are strong predictors of longer Q-LV in LBBB pattern patients. In RBBB pattern the absence of S wave in DI/aVL predicts longer Q-LV. These ECG parameter identify patients who may respond to CRT despite RBBB pattern.

ABSTRACT AB17: CRT: Emerging Methods and Technology

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB17-01

WIRELESS LV ENDOCARDIAL STIMULATION FOR CARDIAC RESYNCHRONIZATION: LONG-TERM (12 MONTH) EXPERIENCE OF CLINICAL EFFICACY AND CLINICAL EVENTS FROM TWO CENTERS

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Introduction: CRT does not always produce the desired clinical outcome due to problematic CS access, lead placement / dislodgement, phrenic nerve stimulation, chronic reliability lead issues, worsening heart failure or high risk ICD / pacemaker upgrades. Endocardial pacing for CRT is an alternative. The Wireless Stimulation of the Endocardium System (WiSE) is comprised of a battery-powered ultrasonic transmitter implanted in a left intercostal space and a leadless pacing electrode fixed directly onto the LV endocardium, replacing the CS lead. The WiSE System was evaluated in the multicenter SELECT-LV study.
Methods: At Homolce and Aalborg Univ. Hospitals, WiSE was implanted in 12 and 10 pts, respectively, who were indicated for CRT, but untreated due to various difficulties. Twenty pts were followed for 12m. Primary and secondary endpoints were evaluated at 1 and 6m.
Results: Baseline characteristics: 19 male; NYHA 2.4±0.7; age 67.3±6.4 yrs; BMI 29.5±4.5; intrinsic and RV paced QRSs were 174±31 ms and 193±23 ms respectively; EF 26.6±6.0%; etiology ICM-10 / NICM-10 / both-2. By 12m, there was 1 death, 1 acute MI, 2 HF admissions in1 pt, and a resolved CVA in 1 pt who had failed to follow the post-op anticoagulation regimen. There were no instances of cardiac perforation or LV electrode dislodgement. Mean implant duration was 534±210 days. Consistent CRT was achieved in 100%, 91% and 94% of pts at 1, 6 and 12m. BiV QRS durations were 133±25, 131±23 and 127±20 ms at 1, 6 and 12m respectively. Reductions in BiV QRS duration compared with the baseline QRS were 40±26, 41±30 and 48±33 ms at 1, 6 and 12m respectively. The 6m clinical composite scores were: 77% improved, 18.6% unchanged and 4.5% worsened.
Conclusions: Wireless endocardial LV pacing is an alternative approach to CRT. These 12m data demonstrate the clinical benefit to our pts, previously untreated by CRT. BiV pacing is maintained with reverse electrical remodeling evident 12m post implant.

AB17-02

LEADLESS LV ENDOCARDIAL STIMULATION FOR CRT: FINAL OUTCOMES OF THE SAFETY AND PERFORMANCE OF ELECTRODES IMPLANTED IN THE LEFT VENTRICLE (SELECT-LV) STUDY

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Aalborg University Hospital, Aalborg, Denmark, Herzzentrum Brandenburg, Bernau/Berlin, Germany, Isala Klinieken, Zwollz, Netherlands, Leiden Univ Medical Center, Leiden, Netherlands, Leiden University Medical Center, Leiden, Netherlands, St. Antonius Ziekenhuis - Cardiology Dept., Nieuwegein, Netherlands

Introduction: Patients indicated for conventional CRT (CRT) do not always benefit due to CS lead issues both acute and chronic, inability to place the lead or not responding to CRT. LV endocardial pacing has been proposed as a potential solution. SELECT-LV assessed the safety and performance of a novel Wireless Stimulation of the Endocardium System, (WiSE), providing endocardial LV stimulation.
Methods: This non-randomized EU study of CRT included pts with either a failure of CRT, or requiring an upgrade and were unsuitable for CRT. WiSE includes a leadless pacing electrode implanted at the endocardial LV free wall. The electrode is activated by a submuscular ultrasonic transmitter, synchronized with RV pacing pulses from a co-implanted pacer/ICD. Primary end points of safety / performance and secondary endpoints for safety / performance / preliminary efficacy were at 1 and 6m.
Results: 39 were enrolled but 3 (8%) of pts did not have an adequate acoustic window, 1 withdrew pre-implant, and 1 had intra-operative VF precluding successful implantation; this pt died a few days later. There were successful implants in 34 of 35 pts (97%), and 34 (97%) pts completed 6m follow-up. Baseline data: age 65±8 yrs; 29 (85%) male; 44% ICM, 44% NICM and 12% both; EF 26.0±6.2; NYHA 2.6±0.6; and baseline intrinsic QRS 170±29 ms. There were 3 (8.5%) AEs peri-operatively and 8 AEs (22%) by 1 month. BiV pacing at 1 and 6m was demonstrated in 33 (97%) of 34 pts and in 31 (94%) of 33 pts respectively. Mean QRS reductions were 51 and 36 ms compared with baseline RV paced QRS and baseline intrinsic QRS respectively. At 6m, 63% of pts demonstrated ≥ 5% increase in EF at 6m; the mean increase was 7.1±8.0%. Compared with baseline, at 6m, 67% pts improved ≥1 NYHA class and 52% patients showed ≥15% improvement in LVESV. The clinical composite score at 6m showed that 28 (85%) improved, 3 (9%) unchanged, and 2 (6%) worsened.
Conclusions: This multicentre experience has demonstrated the feasibility of direct, wireless endocardial LV pacing to achieve CRT in patients with a previous CRT failure or previously unsuitable for CRT.

AB17-03

IN VIVO NON-INVASIVE ULTRASOUND-BASED CARDIAC PACING IN PIGS

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Introduction: Currently, no non-invasive cardiac pacing device acceptable for prolonged use in conscious patients exists. The main approach is invasive, employing intravascular catheters, which has associated risks. Focused ultrasound can be used to perform remote pacing using reversibility of electromechanical coupling of cardiomyocytes. This technique might be useful in the short term in the clinical settings in various conditions: temporary pacing for bradycardia or any clinical condition with risks of asystole; terminating or examining the inducibility of tachyarrhythmia; screening and optimization of cardiac resynchronization therapy. Here we described an extracorporeal cardiac stimulation device and study its efficiency and safety.
Methods: In vivo non-invasive stimulation was performed using 314 sonications in 4 anesthetized pigs using a focused ultrasound device (Image Guided Therapy, France, 256 elements, 13/13 cm aperture/focal, operating at 1 MHz) under MR-guidance (Siemens Avanto 1.5T, Germany). The animals were injected with ultrasound contrast agents using SonoVue (Bracco, Italy. Two consecutive 0.1 mL.kg-1 boli intravenous injections were performed in each animal. At the end of each in vivo experiment, a navigated delayed inversion-recovery 3D Flash sequence was performed. The animals were injected with 0.2 mmol.kg-1 gadoterate meglumine (Dotarem®, Guerbet, France) and scanned 15 minutes post injection. Masson's staining was performed to assess acute damages screening from acoustic stimulation.
Results: Using this setup, consistent cardiac stimulation was achievable for up to 1 hour sessions in 4 different animals. No damage was observed in inversion-recovery MR sequences performed in vivo in the 4 animals. No signal increase can be seen in the myocardium in the delayed-enhancement MR images that would indicate irreversible injury. Histological analysis revealed no differences between stimulated and control regions, for all in vivo cases.
Conclusions: To the best of our knowledge, this study is the first in vivo proof of feasibility of controlled non-invasive ultrasound-based cardiac stimulation in large animals. Preliminary safety results showed that this novel technology offers good prospects for clinical developments.

AB17-04

PERMANENT HIS BUNDLE PACING IS AN EXCELLENT ALTERNATIVE TO CARDIAC RESYNCHRONIZATION THERAPY

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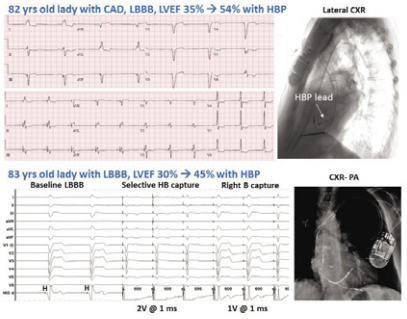
Introduction: Cardiac resynchronization therapy (CRT) is effective in patients with cardiomyopathy, heart failure, LBBB and / or right ventricular pacing. Permanent His bundle pacing (HBP) has been reported to correct LBBB and normalize conduction in patients with AV block. The aim of the study is to assess the feasibility and outcomes of HBP in CRT eligible or failed pts.
Methods: HBP was attempted in patients with previously failed LV lead, non-responders or in pts with AV block as an alternative to CRT. HBP was performed using Medtronic 3830 pacing lead. Implant characteristics, NYHA functional class and LVEF were assessed in follow-up.
Results: HBP was successful in 23 of 25 pts (age 72±14 yrs, male 15, CAD 9, LBBB 13, AV block 12). Indications: failed LV lead 11, non-responder 2, primary HBP 8, combined LV and HBP 4. NYHA functional status improved from 2.9 to 1.6 (p=0.05); LVEF improved from 32±10 to 46±11% (p=0.001); QRS duration decreased from 169±24 ms to 113±17 ms with HBP (P<0.001).
Conclusions: NYHA functional class, LV systolic function and heart failure symptoms improved with HBP. Permanent HBP is an excellent alternative to CRT in patients with failed LV lead, non-responders or as primary option in pts with AV block and heart failure.



AB17-05

WIRELESS LV ENDOCARDIAL STIMULATION FOR CRT, SELECT-LV STUDY: PERFORMANCE AND PRELIMINARY EFFICACY IN ISCHAEMIC PATIENTS

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Introduction: Pts implanted with conventional CRT (CRT) do not always benefit. Inability to place the CS lead, lead instability, and lack of clinical response to CRT are a few causes. Left Ventricular (LV) endocardial pacing has been proposed as a potential solution. The SELECT-LV study assessed the safety and performance of the novel Wireless Stimulation of the Endocardium System, (WiSE), to provide endocardial LV stimulation. This substudy has looked at the outcomes for the ischaemic patients, a difficult group to treat effectively with CRT.
Methods: The SELECT-LV Study is a non-randomized EU study of CRT-indicated pts with either a failure of CRT, or requiring an upgrade but unsuitable for CRT. The WiSE System includes a leadless pacing electrode implanted on the LV free wall. The electrode is activated by a submuscular ultrasonic transmitter synchronized to the RV pacing pulse of a co-implanted pacer/ ICD. The primary efficacy endpoint was successful BiV pacing (verified by EKG) at 1 m; secondary endpoints were performance at 6m together with preliminary efficacy assessment.
Results: Of 34 total pts, 15 had ischaemic cardiomyopathy; all were successfully implanted. Baseline data: age 68±7 yrs, 13 male, EF 24.1±5.6 %, NYHA 2.7±0.6 and baseline intrinsic QRS 168±32 ms. One pt had a revision of battery and transmitter, 1 pt had a CVA, which resolved, after failing to follow the prescribed anticoagulation regimen and another had a groin aneurysm. Consistent BiV pacing was demonstrated in 15 (100%) pts at 1 and 6 m. Reductions in QRS duration from intrinsic baseline at 1 and 6m were 44 and 39 ms, and from the baseline RV paced QRS were 54 and 42 ms. The increase in EF at 6m was 6.4±8.6% with 64.2% pts having ≥5% increase. NYHA class decreased to 1.8±0.8. LV end systolic volume decrease was 15.4±27.8 ml, with 45% and 55% of pts experiencing a 15% and 10% reduction respectively. Clinical composite score, including death, HF hospitalisation and global assessment, improved in 87% (13 pts), was unchanged in 6.6% (1 pt) and worsened in 6.6% (1 pt).
Conclusions: Difficult to treat ischaemic pts implanted in the SELECT-LV study showed promising clinical outcomes.

AB17-06

HIS BUNDLE PACING CAN REVERSE ADVERSE ELECTRICAL AND STRUCTURAL REMODELING INDUCED BY CHRONIC RIGHT VENTRICULAR PACING IN PATIENTS WITH LONGSTANDING COMPLETE HEART BLOCK

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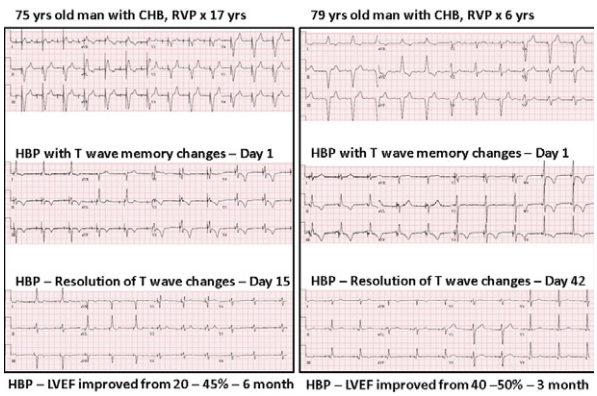
Introduction: His bundle pacing is a physiological alternative to right ventricular pacing (RVP). Adverse electrical and structural remodeling is caused by chronic RVP. The aim of the study is to assess 1) the feasibility of HBP in pts with longstanding complete heart block (L-CHB); 2) reversal of remodeling induced by RVP.
Methods: HBP was attempted in 21 patients (age 74±13 yrs; men 13; HTN 15, DM 4, CAD 7, AF 8, AVR 1, MVR 2, AVN ablation 3) with L-CHB (mean duration 8±6 yrs, range 1-24 yrs) and chronic RVP. HBP was performed using Medtronic SelectSecure 3830 lead delivered via C315His sheath. Indications for HBP: pacing induced cardiomyopathy (PIC) 8, lead failure 8, infection 5.
Results: HBP was successful in all 21 pts. Thirteen patients had AV nodal block and 8 had HV block. Mean fluoroscopy duration 11±6 min. QRS duration significantly narrowed from 181±17 ms (152-222 ms, RVP) to 117±20 ms (85-144 ms, HBP, P<0.001). HBP threshold at implant was 1.8±1.2 V @ 0.5 ms; at last f/u (1.6±1 yr) was 1.75±0.9 V @ 0.5 ms. Ventricular sensing amplitude 4.6±4.4 mV (1.2 - 15 mV). LVEF improved from 32% (range 17-45%) at baseline to 49% (20-64%) during follow-up in the 8 pts with PIC (P=0.01). NYHA functional status improved by at least 1 class in 15 of 21 pts. All pts showed evidence for paradoxical acute T wave memory changes with HBP and normalized in 2-6 weeks.
Conclusions: Permanent HBP was successful in 21 pts with L-CHB and chronic RVP. Despite long duration of CHB (nodal and infra-nodal), conduction through distal HB and normalization of QRS could be achieved with HBP. Chronic RVP induced electrical (depolarization and repolarization) and structural (LV function) changes could be reversed with HBP.



ABSTRACT PLUS AB18:
CRT Insights from Recent Clinical Trials

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB18-01

LEFT VENTRICULAR ELECTRICAL DELAY (QLV) AND REDUCTION IN MITRAL REGURGITATION FOLLOWING CARDIAC RESYNCHRONIZATION THERAPY: MECHANISTIC INSIGHTS FROM THE SMART-AV SUBSTUDY

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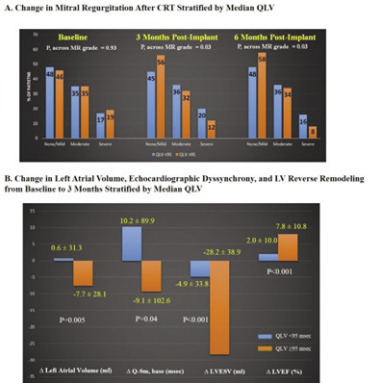
Introduction: We performed a mechanistic analysis of mitral regurgitation (MR) reduction following cardiac resynchronization therapy (CRT) by assessing the relationship between left ventricular (LV) electrical delay (QLV) at the LV stimulation site and MR reduction after CRT.
Methods: The study population (n=426; 66±11 years, male 66%, QRS 153±25 ms, LBBB 75%, LVEF 28±9%) were patients enrolled in the SMART-AV study. QLV was assessed retrospectively in a blinded core lab and defined as the time from QRS onset to LV electrogram peak. A prolonged QLV was defined as ≥ the median value (95 msec). MR was defined using guideline criteria. Echo dyssynchrony was assessed as the maximal difference in time from QRS onset to peak systolic velocity (Q-Sm) across 6 basal segments at baseline, 3 and 6 months after CRT. Logistic regression was used to identify predictors of MR grade reduction at 6 month follow up with multivariable adjustment including baseline LVESV and MR grade.
Results: MR grade was similar between QLV groups at baseline but significantly lower in patients with longer QLV at 3 and 6 months (Figure, A). At 3 months, longer QLV was associated with reductions in LA volume and echo dyssynchrony as well as LV reverse remodeling (LV-RR) (Figure, B). Increasing baseline QLV was associated with MR grade reduction at 6 months (adj HR 1.133 [1.03-1.25] / 10ms increase QLV; p=0.02). Three-month ΔLVESV (p<0.001) but not 3-month ΔQ-Sm (p=0.5) was associated with 6-month MR reduction.
Conclusions: In patients undergoing CRT, longer QLV was associated with echo resynchronization, LV-RR, and MR reduction - all apparent at 3 months. The mechanism of QLV associated MR reduction appears most related to LV-RR.



AB18-02

CARDIAC RESYNCHRONIZATION THERAPY COMBINED WITH CORONARY ARTERY BYPASS GRAFTING IN ISCHEMIC HEART FAILURE PATIENTS: LONG-TERM RESULTS OF THE RESCUE STUDY

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Introduction: Totally epicardial cardiac resynchronization therapy (CRT) is a novel treatment modality for patients with heart failure and systolic dyssynchrony undergoing coronary artery bypass grafting (CABG). In this study we have prospectively evaluated the long-term outcomes of totally epicardial CRT.
Methods: Between September 2007 and June 2009, one hundred seventy eight patients were randomly assigned to the CABG alone group (n=87) and CABG with concomitant epicardial CRT implantation (n=91). The primary endpoint of the study was all-cause mortality in the two groups between the day of surgery and August 13, 2013 (common closing date). The secondary outcomes included mode of death, adverse cardiac events and lead performance.
Results: The mean follow-up was 55±10.7 months. According to per-protocol analysis with treatment as a time-dependent variable to account for conversion from CABG to CABG+CRT, there were 24 deaths (35.8%) in the CABG group and 17 deaths (15.3 %) in the CABG+CRT group. As compared to CABG alone, concomitant CRT was associated with reduced risk of both all-cause mortality (hazard ratio (HR) 0.43, 95% confidence interval (CI) 0.23 to 0.84, p=0.012) and cardiac death (HR 0.39, 95% CI 0.21 to 0.72, p=0.002). Eleven (12.6%) sudden deaths were observed in the CABG group in comparison to 4 (4.4%) in the CABG+CRT group (p=0.048). Hospital re-admission was required for 9 (9.9%) patients in CABG + CRT group and for 25 (28.7%) patients in CABG group (p=0.001). There were 4 (1.5%) epicardial lead failures.
Conclusions: The results of our study suggest that the procedure of coronary artery bypass grafting and totally epicardial CRT system implantation is safe and significantly improves the survival of patients with heart failure and dyssynchrony during long-term follow up.

AB18-03

EARLY AV NODE ABLATION VERSUS PHARMACOLOGICAL RATE CONTROL IN PATIENTS WITH CRT AND AF. RESULTS OF SPARE III, A RANDOMIZED MULTICENTER STUDY

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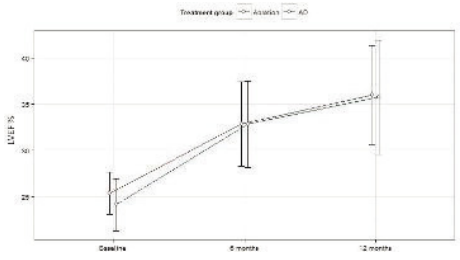
Hospital Universitari Vall d'Hebrón, Barcelona, Spain, Hospital Clinic, Universitat de Barcelona., Barcelona, Spain

Introduction: Maximum ventricular pacing (VP) is necessary for good CRT response. In AF AV node ablation is recommended. The aim of the study was to analyze whether early AV node ablation (EAVNA) in patients with AF submitted to CRT improved response to therapy.
Methods: A multicenter randomized trial analyzed a cohort of patients with AF treated with CRT. Inclusion criteria were: AF, NYHA III-IV, QRS >120 ms and LVEV ≤35%. Patients with AF and fast, uncontrolled heart rate (HR) or patients with AF and slow heart rate requiring ventricular pacing were excluded. After successful CRT implant, patients were randomized to EAVNA or medical therapy (MT) to slow HR. All patients underwent clinical and echocardiographic evaluation prior to implantation and at 6- and 12-month follow-up. Responders were defined as survivors at 12 months post-implant with ≥10% LVESV reduction without requiring heart transplant.
Results: A group of 60 patients was randomized to EAVNA (30) or MT (30). The percentage of VP at 6 and 12 months was 99% and 99% respectively, in the EAVNA group and 95% and in the MT group (p: NS). During follow-up, 20% of patients from the MT crossed over to AV node ablation. At 12 months, there was no difference between groups in the percentage of responders: 12/30 (40%) EAVNA vs. 10/30 (33%) MT (RR 1.2, 95% CI [0.6-2.3], p=0.79). LVEF improvement was similar too. In each group 2/30 patients died (6.6% mortality);1 patient from EAVNA required heart transplant. Hospital admissions were also similar between study groups: 8/30 (26.6%) EAVNA and 8/30 (26.6%) MT.
Conclusions: Compared to MT a strategy of EAVNA in patients with CRT and AF did not improve CRT response or clinical improvement.



AB18-04

ECHOCARDIOGRAPHY VS NON-INVASIVE HEMODYNAMIC OPTIMIZATION OF AV AND VV DELAY FOR CARDIAC RESYNCHRONIZATION THERAPY: THE PROSPECTIVE, MULTI-CENTRE, RANDOMIZED, CROSS-OVER, NON-INFERIORITY BRAVO STUDY.BRITISH RANDOMIZED CONTROLLED TRIAL OF AV AND VV OPTIMIZATION ("BRAVO") STUDY

Zachary I. Whinnett, MBBS, PhD, Daniel Keene, MRCP, Prapa Kanagaratnam, PhD, MRCP, Mark Tanner, MD, Edward Duncan, PhD, MRCP, Martin Lowe, PhD, FRCP, Mark Dayer, PhD, FRCP, Philip Moore, PhD, MRCP, Francisco Leyva, MD, FRCP, Mike Frenneaux, MD, FRCP, Mark Mason, FRCP, Alun D. Hughes, MBBS, PhD and Darrel Francis, MD, FRCP. Imperial College London, London, United Kingdom, Western Sussex Hospitals NHS Foundation Trust, West Sussex, United Kingdom, University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom, Barts and The London NHS Trust, London, United Kingdom, Taunton and Somerset NHS Foundation Trust, London, United Kingdom, West Hertfordshire Hospitals NHS Trust, Watford, United Kingdom, University Hospital Birmingham, Birmingham, United Kingdom, University of Aberdeen, Aberdeen, United Kingdom, Royal Brompton and Harefield NHS Foundation Trust, London, United Kingdom

Introduction: Landmark studies of biventricular pacing performed atrioventricular (AV) delay optimization, but the process requires considerable time of expert staff. BRAVO is a multi-centre, randomized, cross-over, non-inferiority trial comparing echocardiographic optimization of AV and interventricular (VV) delay with an alternative method using non-invasive blood pressure that can be automated to consume less staff resources.
Methods: Patients with a previously implanted cardiac resynchronization devices were recruited and allocated to six months in each arm in random order. In the echocardiographic arm, AV delay was optimized by the iterative method, and VV delay by maximizing LVOT VTI. In the haemodynamic arm AV and VV delay were optimized using non-invasive blood pressure measured using finger photoplethysmography. At the end of each 6-month arm, the primary outcome was measured, objective exercise capacity quantified as peak oxygen uptake (VO2) during cardiopulmonary exercise testing. Secondary outcome measures were echo measurement of left ventricular remodelling, quality of life scores and NT-proBNP.
Results: 401 patients were enrolled, median age 69 years, 78% male, NYHA class II 84%, III 16%. There was no significant difference in VO2 after 6 months with Echo optimized settings compared with hemodynamic optimized settings (mean difference 23 ml/min, P=0.7). There was also no significant difference in LV volumes, symptoms or hormonal secondary endpoints: mean change in LV systolic dimension 1mm P= 0.18, LV diastolic dimension 0 mm (P=0.93), Minnesota score -2 (P=0.06), SF36 0.40 (P=0.6), and NT-proBNP -10 pg/mL (P=0.9).
Conclusions: Optimization of AV and VV delay of CRT devices using non-invasive blood pressure is non-inferior to echocardiographic optimization. Therefore non-invasive haemodynamic optimization is an acceptable alternative, which has the potential to be automated and therefore more easily implemented.

AB18-05

OUTCOMES OF CARDIAC RESYNCHRONIZATION THERAPY IN PATIENTS WITH INTERMITTENT ATRIAL ARRHYTHMIAS IN THE COMPANION TRIAL

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Introduction: In mild heart failure, intermittent atrial arrhythmias (IAA) do not seem to attenuate the benefit of cardiac resynchronization therapy (CRT). In this study, we report CRT outcomes in patients with advanced heart failure and IAA from the COMPANION trial.
Methods: The COMPANION trial randomized 1520 subjects with advanced heart failure and sinus rhythm at randomization to optimal pharmacologic therapy (OPT, n = 308) or CRT without (CRT-P, n = 617) or with (CRT-D, n = 595) defibrillation. In this analysis, event driven outcomes in patients with no history of baseline arrhythmia (b-NoAF/AFL) and those with a history of intermittent atrial fibrillation or atrial flutter at baseline (b-IAF/AFL) were assessed. Outcomes in patients who developed in-

trial atrial fibrillation or flutter (it-AF/AFL) were also evaluated.
Results: The b-NoAF/AFL and b-IAF/AFL groups consisted of 887 and 293 subjects, respectively; 340 subjects had unclassified atrial arrhythmias at baseline and were excluded from analysis. In the b-NoAF/AFL group, compared to OPT the CRT-P/D arms combined exhibited a significant reduction in the primary endpoint of all-cause mortality or all cause hospitalizations: Hazard ratio (HzR) 0.73, p = 0.002. When analyzed separately, CRT-P and CRT-D each resulted in significant reductions in mortality compared to OPT (CRT-P HzR 0.67, p = 0.04; CRT-D HzR 0.66, p = 0.04). However, in the b-IAF/AFL group, CRT-P/D combined did not result in a significant reduction in the primary endpoint (HzR 1.16, p = 0.38) or in mortality alone (CRT-P HzR 1.28, p = 0.44; CRT-D HzR 0.94: p = 0.85). In 150 subjects who developed it-AF/AFL based on adverse event reporting, the annualized incidence of it-AF/AFL was significantly higher in the b-IAF/AFL group compared to b-NoAF/AFL (19.4% versus 6.6%, p < 0.001). In the 71 subjects from the b-NoAF/AFL group who developed it-AF/AFL, the effect of CRT-P/D on the primary endpoint was significantly attenuated compared to the 644 subjects who did not develop it-AF/AFL (HR: 1.46, p = 0.008).
Conclusions: In the COMPANION trial, compared to the OPT, no CRT control group the effect of CRT-P/D was attenuated in patients with a history of intermittent AF/AFL. This finding may have implications for CRT patient selection.

ABSTRACT PLUS AB19: Sports, Devices, and Arrhythmias: Managing Children in the 21st Century

Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB19-01

SAFETY OF SPORTS FOR YOUNG PATIENTS WITH ICDS: LONG-TERM RESULTS OF THE MULTINATIONAL ICD SPORTS REGISTRY

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Introduction: Despite safety concerns young patients with ICDs participate in sports. We undertook a prospective multinational registry to determine the incidence of serious adverse events due to sports participation. The primary endpoint was death or resuscitated arrest during sports, or injury during sports due to arrhythmic symptoms and/or shock. Secondary endpoints included system malfunction and incidence of ventricular arrhythmias requiring multiple shocks for termination.
Methods: Athletes with ICDs age < 21 years were included in this post-hoc sub-analysis. Data on sports and clinical outcomes were obtained by phone interview and medical records. ICD activations and clinical details of lead malfunction were classified by two electrophysiologists.
Results: A total of 129 young athletes < 21 years of age participating in competitive (N=117) or dangerous (N=12) sports were enrolled. Median age was 17 years (range 10-21, mean 16, 40% female, 92% Caucasian. Most common diagnoses were long QT syndrome (N=49), HCM (N=30), and congenital heart disease (N=16). Most common sports were basketball and soccer, including 79 varsity/JV high school and college athletes. Other sports included football, rock climbing, scuba diving, skiing and others. Over a median follow-up of 42 months, (iqr 25-49), 35 (27%) of athletes received 39 shocks (table). There were no occurrences of either primary endpoint. There was one VT/VF storm during competition. Freedom from lead malfunction was 92.3% at 5 years and 79.6% at 10 years.
Conclusions: While shocks related to competition/practice are not uncommon, there were no serious adverse sequelae. Lead malfunction rates were similar to previously reported.

Table: Shock events. Values refer to events.

Rhythm	Competition related*	Physical activity related†	Other	Total
VT	1	4	3	8
VF	3	3	5	11
AF	1	2	0	3
Noise	0	3	3	6
Other SVT	2	1	1	4
T wave oversensing	2	1	2	5
AF/SVT storm	0	1	0	1
VT/VF storm	1	0	0	1
Total	10	15	14	39

*Includes competition, post-competition, or practice for competition; †includes post-physical activity.

AB19-02

USE OF DOFETILIDE IN ADULT PATIENTS WITH ATRIAL ARRHYTHMIAS AND CONGENITAL HEART DISEASE: A PACES MULTI INSTITUTIONAL COLLABORATIVE STUDY

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Introduction: Arrhythmia management has become the major treatment challenge in adult patients with congenital heart disease (ACHD). We sought to investigate the efficacy and safety profile of dofetilide for atrial arrhythmias in this patient population.
Methods: A multicenter retrospective chart review was performed. We included patients (age ≥ 18) with ACHD who had refractory atrial arrhythmias treated with dofetilide (2008-2014).
Results: We identified 49 patients with a mean age at initiation of 45 ± 6 years. ACHD type included transposition of great

arteries (12), single ventricle (8), ASD (8), tetralogy of Fallot (6), AV canal (4), mitral/aortic stenosis (5) and other (6). Thirty-three (66%) had atrial fibrillation (AF) and 16 (33%) had intra-atrial reentrant tachycardia (IART). Pre-initiation QTc was 458 ± 36 ms and post-initiation QTc was 491 ± 41 ms (P<0.001). A total of 17 (35%) patients had inpatient adverse events: torsades (1), sinus node dysfunction (1), ventricular tachycardia (1), excessive QTc prolongation requiring dose reduction (15) and QTc prolongation requiring discontinuation (1). There was no difference in adverse events in patients with IART compared to patient with AF (56% vs. 24%, p=0.053) or between high dosing (500 mcg BID) and low dosing (125-250 mcg BID) (39% vs. 29%, p=0.55). One patient discontinued therapy prior to discharge due to persistent arrhythmia. Of the patients who were discharged on dofetilide (n=44), 33 (75%) had adequate rhythm control and 11 (25%) had partial rhythm control. Starting dose was associated with adequate rhythm control (high v. low: 89% v. 56%, p=0.03). After a mean follow up of 3.2 ± 2.5 years, 21 (48%) patients remained on dofetilide with resolution or improvement of atrial arrhythmias and 4 patients died. Reasons for discontinuation include: waning effect (11), anxiety (1), noncompliance (2), successful ablation (2) and unknown (3).
Conclusions: Dofetilide appears to have a similar efficacy and safety profile in patients with ACHD compared to patients without. Dofetilide should be considered in patients with ACHD and refractory atrial arrhythmias.

AB19-03

CARDIAC RESYNCHRONIZATION THERAPY IN PATIENTS WITH FONTAN PHYSIOLOGY AND HEART BLOCK

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Introduction: Heart block in patients (pts) with single ventricle physiology palliated to a Fontan increases their morbidity and mortality. The effect of cardiac resynchronization therapy (CRT) in this pt population is unclear.
Methods: Retrospective review of all Fontan pts being paced for heart block at a single institution between 1990 and 2015. Multisite pacing (i.e. CRT) was achieved using epicardial leads placed in an anterior-posterior orientation. Qualitative ventricular function was classified as "normal" (normal function or mild dysfunction) or "abnormal" (moderate to severe dysfunction).
Results: Over the last 25 years, 169 pts with single ventricle physiology palliated to a Fontan underwent ventricular (V) pacing for high-grade to complete heart block. 26 pts underwent CRT (median age 15 years, IQR 5-27 years), 10 of which were primary CRT devices (i.e. not V-paced prior). For CRT pts, 4 (15%) died or underwent transplant (3 were primary CRT), compared to 25 (20%) in the non-CRT group (p=0.6). At latest follow-up (median age 19 years, IQR 11-29 years), 10 (38%) CRT pts had abnormal function compared to 27 (21%) in the non-CRT group (p=0.07). When comparing ventricular function pre- and post-CRT (median follow-up 4.5 years post-CRT, IQR 0.6-5 years), primary CRT devices noted improvement in 1 pt, no change in 8 pts (7 normal function, 1 abnormal), and worsening in 1 pt. In secondary CRT devices, 2 pts improved and 14 had no change (7 normal function, 7 abnormal function). Of the 3 (11%) pts who improved, 2 were single left ventricles and 1 was a single right ventricle.
Conclusions: Dual-chamber pacing using multisite ventricular leads in Fontan pts with heart block did not appear superior to a single site ventricular lead in preventing/reversing ventricular dysfunction using current methodology. More exact techniques for lead positioning need to be explored.

AB19-04

PATIENT CHARACTERISTICS AND RISK OF RECURRENCE DURING TREATMENT AND FOLLOWING ANTI-ARRHYTHMIC WEAN — CAN WE WEAN INFANTS WITH SVT EARLIER THAN ONE YEAR?

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Introduction: Infants with supraventricular tachycardia (SVT) are commonly treated with medications for approximately one year. Whether these infants can be weaned off medications sooner has not been determined. In an effort to help delineate whether a subpopulation of infants can be weaned earlier, we sought to evaluate a large cohort of neonatal SVT, describe patient characteristics, rates, timing and predictors of recurrence.
Methods: Retrospective single-center review of infants <1 yr admitted for re-entrant SVT between 1984-2014. Patients with congenital heart disease were excluded. Follow-up was performed via prospective phone survey investigating recurrence. Analysis for risk of recurrence included: 1) age at presentation, 2) gender, 3) race, 4) history of fetal SVT, 5) Wolff-Parkinson-White (WPW) syndrome, 6) need for >1 oral anti-arrhythmic (AA), 7) ventricular dysfunction at diagnosis, and 8) SVT recurrence during treatment with AA.
Results: Over a 30 year period, 330 infants (205 Male, 62%) were diagnosed at a mean age of 35 days with 85% presenting at <2months of age. WPW was diagnosed in 88 (28%). While on AA treatment, documented SVT recurrence occurred in 57 (17%), occurring <2 months in 49%, <4 months in 60%, <6 months in 69% and <9 months in 76%. Among 171 patients with ≥1 year follow up after discontinuation of AA (mean follow up 8 yrs ± 6 yrs), 18% recurred. Of these, 44% recurred by age 2 yrs, 64% by 3 yrs and 81% by 5 yrs of age. 49 patients (15%) underwent eventual catheter ablation. On multivariate analysis, factors associated with risk of recurrence during AA treatment include WPW (p<0.001) and need for >1AA (p<0.001). Risk of recurrence after discontinuation of AA include history of fetal SVT (p=0.011), WPW (p=0.001), need for >1 oral AA (p=0.001).
Conclusions: A majority of infants with SVT will present within 2 months of life and will not have a recurrence even after weaning from AA. After discontinuation of AA, presence of WPW, need for >1 AA, and history of fetal SVT appear to be risk factors for recurrence. A subpopulation of infants without these risk factors may be amenable to earlier antiarrhythmic wean.

AB19-05

RISK OF DEATH FROM CARDIAC ARREST IN PEDIATRIC HEART TRANSPLANT RECIPIENTS: QUERY OF THE UNOS DATABASE

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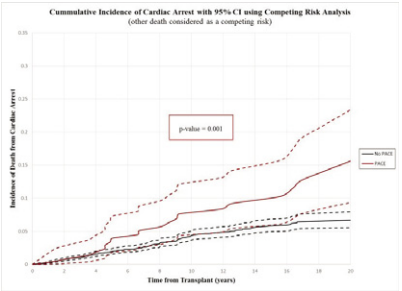
Introduction: Death due to cardiac arrest (CA) after heart transplantation occurs in 10-20% of adults. Risk factors include systolic dysfunction, rejection, and cardiac allograft vasculopathy. The incidence and risk factors for CA in pediatric heart transplant (PHTx) recipients is not well known. This study's objectives were to determine the incidence and risk factors for CA in PHTx recipients, and whether a pacemaker (PM) affects survival.

Methods: This was a retrospective study including patients transplanted at ≤ 18 years using the United Network for Organ Sharing (UNOS) registry. Kaplan-Meier and multivariate analysis were performed.
Results: There were 7,719 patients ≤ 18 years of age transplanted between 1987-2013, and of these 2,637 patients (34%) died. Death was due to CA in 11% (n = 298). PM was placed in 7% after transplantation. A multivariate risk analysis was done in 1848 patients with complete data. From this group, 40 patients died from CA (2%) and 193 had a PM (10%). Risk factors associated with CA included increasing class I panel reactive antibodies (PRA) at time of PHTx (hazard ratio [HR] 1.02 per percent point increase, p < 0.001), ejection fraction ≤ 40% at any time post-transplant (HR 6.5, p < 0.001), and presence of a PM (HR 3.5, p = 0.02). In total, there were 234 (3%) patients with a PM after PHTx, and 91 (39%) died. Cause of death was CA in 22 (24%) patients. A competing risk analysis of CA in patients with/without a PM showed worse survival in the PM group (p = 0.001) (Figure).
Conclusions: Increasing class I PRAs at time of transplant, systolic dysfunction, and presence of a PM increase the risk for CA. The presence of a PM does not seem to confer protection to this population.



ABSTRACT AB20:
Provocative ICD Cases: Innovative Bailout Options for Therapeutic Dilemmas

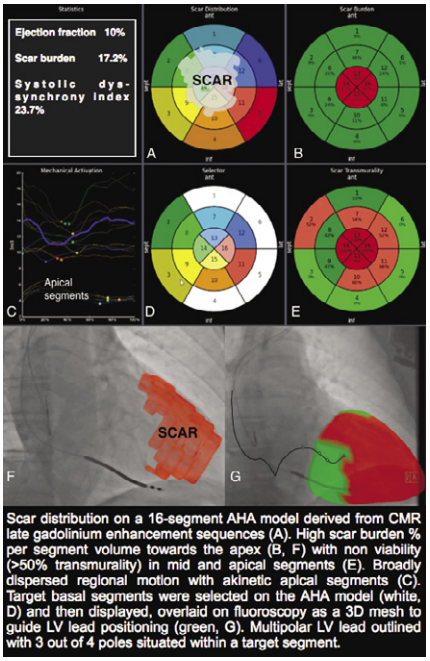
Thursday, May 5, 2016
1:30 PM - 3:00 PM

AB20-01

REAL-TIME INTEGRATION OF CARDIAC MRI TO TARGET LV LEAD IMPLANTATION IN A PATIENT WITH ISCHEMIC CARDIOMYOPATHY, HIGH SCAR BURDEN AND A PREVIOUSLY FAILED IMPLANT

Jonathan M. Behar, MRCP, Peter Mountney, PhD, Antonis Antoniades, MBBS, Daniel Toth, MSc, Sabrina Reiml, BSc, Maria Panayiotou, PhD, Tom Jackson, MRCP, Simon Claridge, MRCP, Bradley Porter, MRCP, Mark O›Neill, DPhil, MD, FHRS, Alexander Brost, PhD, Kawal Rhode, PhD, Reza Razavi, MD, FRCP and Christopher Aldo Rinaldi, MD, FHRS. Imaging Sciences, Kings College London & Guy›s and St Thomas› NHS Foundation Trust, London, United Kingdom, Siemens Healthcare, London, United Kingdom

Introduction: Extensive myocardial fibrosis can limit the positioning of the left ventricular (LV) lead due to high capture thresholds when delivering cardiac resynchronization therapy (CRT). Large scar burden is also associated with less volumetric remodelling and poor clinical response to CRT. Cardiac magnetic resonance (CMR) is the gold standard for delineating myocardial fibrosis; integration of this data onto live fluoroscopy may be clinically useful in difficult implants.
Methods: N/A.
Results: A 72 year old man with ischaemic cardiomyopathy (QRSd 164ms) had a previously failed CRT device insertion; coronary venous anatomy was challenging and capture thresholds were high with a high frequency of phrenic nerve stimulation. A 3D-CMR derived LV shell and scar mesh were segmented and fused with fluoroscopy during a reattempt. Visualization of extensive mid to apical fibrosis with >50% transmurality allowed preferential targeting of non scar segments with late mechanical activation (green, Figure). Biventricular stimulation using poles within the target produced low capture thresholds (<1.5V) with paced QRS duration 138ms compared with intermittent capture (at maximal output 10V) in scarred segments.
Conclusions: Accurate and real-time image fusion utilizing the patients own cardiac anatomy and physiology may have clinical utility in guiding LV lead placement away from scar in order to improve the delivery of CRT.



Scar distribution on a 16-segment AHA model derived from CMR late gadolinium enhancement sequences (A). High scar burden % per segment volume towards the apex (B, F) with non viability (>50% transmurality) in mid and apical segments (E). Broadly dispersed regional motion with akinetic apical segments (C). Target basal segments were selected on the AHA model (white, D) and then displayed, overlaid on fluoroscopy as a 3D mesh to guide LV lead positioning (green, G). Multipolar LV lead outlined with 3 out of 4 poles situated within a target segment.

AB20-02

FAILED MAXIMAL DEFIBRILLATION THRESHOLD TESTING IN THE SUBCUTANEOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATOR

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Introduction: The subcutaneous implantable cardioverter defibrillator (SICD) has emerged as a technological advance to prevent sudden cardiac death in patients who are not pacemaker dependent. The SICD offers the advantage of extracardiac route of implantation and long term lead management options in high risk patients for infection while sustaining non-inferior discrimination of arrhythmia.
Methods: N/A.
Results: A 42-year-old gentleman with a nonischemic dilated cardiomyopathy (EF=20%) on guideline driven medical therapy

for nine months was seen for risk stratification of sudden cardiac death. He had a chronic thromboembolic hematologic disorder and upper extremity deep venous thromboemboli with failed left sided transvenous ICD implantation due to venous occlusion. Given patient preference, implantation indication and consideration of thrombotic potential a SICD was implanted. After successful induction of VF at 50 Hz via the device therapy at 65J and 80J failed to defibrillate the patient warranting external defibrillation which was successful. The shock impedance was 125 ohms demonstrating a tissue interface. The patient received an erect PA radiograph which demonstrated shifting of the shocking coil and can below the diaphragm despite supine positioning via fluoroscopy. The system was revised moving the coil rightward of the sternum to compensate for anatomic shifting and the generator was moved superior above the diaphragm. Defibrillation at 80 J was successful, however upon second attempt this was unsuccessful. Shock impedance was within normal limits on both attempts. Given the probalistic mechanism of DFT's, a JR4 guide catheter was placed transfemoral and identified a patent right sided venous system. A transvenous dual coil ICD was subsequently implanted with DFT's < or = to 25J. The SICD was explanted and the patient was discharged the next day. Analysis of the device by the manufacturer did not demonstrate defect.
Conclusions: This case illustrates the limitations of the SICD and may identify a patient population which can pose challenges in clinical decision making based upon indication of the SICD, patient preference and limitations of current technology.

AB20-03

DEATH OF A PATIENT WITH VT BELOW THE PROGRAMMED ICD DETECTION RATE

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Introduction: Several recent studies have shown that ICDs programmed with high detection rates and/or delayed therapy decrease inappropriate shocks, without an increased risk of mortality. Though specific practice varies, current practice trends are based on the concept that high detection rates are generally safe in patients with ICDs for primary prevention.
Methods: N/A
Results: A 65 year old man with complex medical history including ischemic cardiomyopathy (LVEF 35%) with peripheral vascular disease, end-stage renal disease on peritoneal dialysis and sinus node dysfunction received a dual chamber ICD for primary prevention. He was on optimal medical therapy and followed regularly in the heart failure clinic. The ICD was programmed AAIDDD 60-130 bpm with a VT monitor zone at 171 bpm and a single therapy zone of 194 bpm with the number of intervals for detection at 24/32. He paces in the right atrium 41% of the time and 10% in the right ventricle.
The pacemaker clinic received a remote transmission for multiple episodes of non-sustained VT. He had no ventricular arrhythmias on a device check 1 month earlier. A review of the EGM revealed sustained VT with some cycle length variability, and rates of about 191 bpm intermittently straddling the VT cutoff zone. The rhythm degenerates to a sinusoidal wave form below the rate cutoff. No ICD shocks were delivered. A call to his home reveals that he collapsed suddenly and died earlier that morning. He was seemingly well without complaint prior to the witnessed event. He could not be resuscitated by emergency personnel called to the scene.
Conclusions: This patient died with sustained VT that was just slower than his programmed ICD detection rate and so no therapies were delivered. Whether delivery of ICD therapy would have saved him is unclear, but the fact he was without complaint prior to the sudden death suggests the untreated arrhythmia was the primary cause of death. Although current practice utilizing high detection cutoffs to 200 bpm appears safe generally, there may be some risks to this approach, and further refinement of our concepts of optimal programming may be required to prevent similar outcomes in occasional other patients.

AB20-04

TOO LARGE A LEAD VEGETATION? ANGIOVAC IT!

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Introduction: Insertion of Cardiac Implantable Electronic Devices (CIED) is associated with an increased risk of endocarditis. Surgical extraction is the preferred approach for infected CIED leads with large vegetations. However, literature on removal of large right atrial vegetations using vaccum-assisted thrombectomy devices is very limited. We describe a case of a large right atrial lead vegetation debulked with Angiovac(Angiodynamics, NY, USA) prior to lead extraction with laser sheaths.
Methods: N/A
Results: A 58-year-old man with previous history of non-ischemic cardiomyopathy and ejection fraction of 30%, status post Dual Chamber Implantable Cardioverter-Defibrillator(ICD) placement was admitted for chills and fatigue. On exam he was tachycardic, hypotensive and had an ejection systolic murmur over the left sternal border. A transthoracic echocardiogram(TTE) showed a mobile, echogenic mass attached to the right atrial lead. Transesophageal echocardiogram(TEE) confirmed the presence of a 32x17mm vegetation, prolapsing across the tricuspid valve. The patient was started on broad spectrum antibiotics. Given his poor hemodynamics as well as the risk of embolization from the large vegetation, a percutaneous approach was adopted. AngioVac catheter was guided into the right atrium through a 26 F sheath via the right internal jugular vein. TEE was used to guide the AngioVac catheter to the vegetation and 3-4 large pieces of debris were suctioned into the collecting canister. After confirming complete debulking of the vegetation both leads were extracted using Spectranetics laser sheaths. Pathology samples confirmed bacterial endocarditis and he was discharged home stable on long term antibiotics.
Conclusions: Infection of the CIED leads is a perilous complication requiring total lead extraction. ACC/AHA/HRS guidelines recommend prompt extraction of the infected leads and surgical approach for removal of vegetations >3cm.
Our patient had a successful removal of a large right atrial lead vegetation by Angiovac prior to lead extraction. Hence, in patients at high risk for open heart surgery, a combined technique, using an Angiovac for vegetation removal followed by lead extraction with laser sheaths holds promise to be a safe and effective tool.

AB20-05

R-WAVE AMPLITUDE VARIATION LEADING TO INAPPROPRIATE S-ICD THERAPY-ANOTHER CHALLENGE IN DEVICE MANAGEMENT

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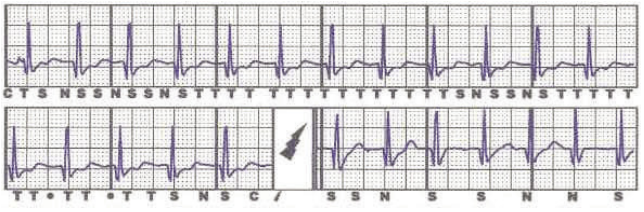
Introduction: The subcutaneous ICD (S-ICD) provides protection against SCD without the risks associated with endocardial leads. The safety, efficacy and rate of inappropriate shocks (IAS) of S-ICD is comparable to that of transvenous

ICD (TV-ICD). The most common cause of IAS is T-wave oversensing (TWOS). We report a rare event in a patient with S-ICD receiving IAS due to increased R-wave amplitude after implant despite appropriate initial screening.
Methods: N/A
Results: A 24-year-old female with familial cardiomyopathy received an S-ICD 5 weeks post-partum. She previously had a TV-ICD implanted at the age of 13 with device malfunction due to lead fracture. Given the patient's age, no pacing indication and unwillingness to proceed with lead extraction, an S-ICD was considered an appropriate choice. The QRS amplitude was large in the S-ICD primary vector but within acceptable limits. Her labs were within normal range. She returned 1 week later with IAS. Her QRS amplitude was noted to have increased since the implant exceeding the device-sensing algorithm, leading to a downward shift in the baseline and predisposing to oversensing (Figure). An alternate vector with the smallest QRS was selected to overcome this problem and exercise testing was performed to optimize device function.
Conclusions: Although IAS are more commonly due to TWOS as a result of a relatively low-amplitude R-wave and large T-wave, IAS due to large R-waves has not been reported. No software upgrade is available to resolve this problem in the current generation device. Until a more dynamic range of R-wave amplitude sensing is permitted, selection of an alternate vector with smaller R-waves should resolve this problem.



AB20-06

INAPPROPRIATE SHOCK DELIVERY FROM SUBCUTANEOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATOR SYSTEMS DUE TO EARLY REDUCTION IN VENTRICULAR ELECTROGRAM AMPLITUDE

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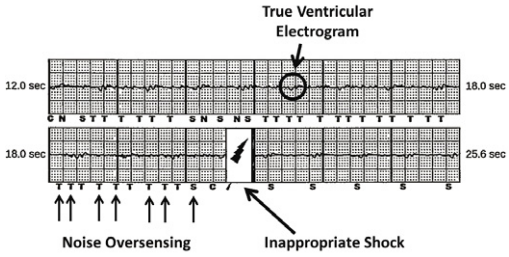
Introduction: The subcutaneous ICD (S-ICD) detects ventricular activity using one of 3 sensing vectors from 3 electrodes on the lead and generator. The device employs non-programmable algorithms to detect ventricular rate and discriminate SVT from VT or VF. We present 2 patients who passed the pre-operative ECG screening and had good sensing vectors at S-ICD implantation, but who received inappropriate shocks due to subsequent markedly reduced R wave amplitude and oversensing.
Methods: N/A
Results: A 47 yo woman with renal failure on dialysis, bifascicular block (QRS 160 ms) and non-ischemic cardiomyopathy (EF 20%) had a VF arrest. Transvenous ICD implantation was not feasible due to R-sided venous occlusion and a L-sided dialysis fistula, so she underwent S-ICD implantation. One week later, she received multiple inappropriate shocks for noise oversensing in the setting of markedly reduced R wave amplitudes, both lying and standing. A 49 yo man with non-ischemic cardiomyopathy (EF 35%) had a VF arrest and underwent S-ICD implantation. One month later, while mopping the floor, he received a shock from his device. Interrogation revealed an inappropriate shock from markedly reduced R wave amplitude and noise oversensing. Small R waves in his optimal sensing vector were reproduced with bending forward.
Conclusions: Despite a favorable auto-selected sensing vector at implantation, R wave amplitudes can subsequently drop, leading to undersensing, oversensing, and inappropriate shocks. There are minimal programming options to overcome this problem when it occurs, and reoperation for electrode repositioning or conversion to a standard ICD are the primary available solutions.



ABSTRACT AB21: Clinical Research Abstracts

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB21-01

INJECTABLE LOOP RECORDER IMPLANTATION IN A NON-EP LAB SETTING: ANALYSIS OF COMPLICATION RATES

Natalia Young, PA, Ann E. Barnett, PA, Michael E. Field, MD, FHRS, Miguel A. Leal, MD, Douglas E. Kopp, MD, Ryan Kipp, MD, Lee L. Eckhardt, MD, FHRS, Kurt Hoffmayer, MD and Jennifer M. Wright, MD. University of Wisconsin Hospital and Clinics, Madison, WI, University of Wisconsin School of Medicine, Madison, WI, University of Wisconsin, Madison, WI, Univ of Wisconsin Hospital and Clinics, Madison, WI, University of Wisconsin Hospitals and Clinics, Madison, WI, University of Wisconsin Hospital Clinics, Madison, WI

Introduction: Implantable loop recorder insertion (ILR) has historically been performed in the cardiac catheterization or electrophysiology lab, or operating room. The newest generation loop recorder (Medtronic Reveal LINQ™) is injectable with potential for implantation in a non-EP lab setting facilitating improved workflow and resource utilization. We report our experience with injectable ILR placement in the non-EP lab setting.
Methods: A retrospective review was performed including all patients referred for injectable ILR placement from March 2014 to November 2015. All device placement procedures were performed in a procedure prep and recovery unit using the standard manufacturer deployment kit with sterile technique and local anesthetic following a single dose of intravenous antibiotic. Acute procedural success and complication rates following injectable ILR placement in the ambulatory setting were reviewed.
Results: During the study period 139 injectable ILRs were implanted. Acute procedural success with adequate sensing occurred in 100% of patients. Complications occurred in 1.4% of implantations (one infection and one device erosion). Two patients received device explant due to pain at the device site. No other complications were observed.
Conclusions: In this retrospective single center study,

implantation of injectable ILR in a non-EP lab setting following a single dose of intravenous antibiotic and standard manufacturer technique yielded a low complication rate. Use of this implantation strategy may improve EP lab workflow while providing a safe and effective technique for device placement.

AB21-02

IMPELLA PERCUTANEOUS VENTRICULAR ASSIST DEVICE USE IN VENTRICULAR TACHYCARDIA CATHETER ABLATION: A FOUR-YEAR SINGLE-CENTER EXPERIENCE

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Introduction: Impella percutaneous ventricular assist device (PVAD) has been used during radiofrequency catheter ablation (RFA) of ventricular tachycardia (VT) in patients at risk for acute hemodynamic decompensation in an attempt to improve the outcomes of VT RFA. Prior studies have shown that its use is safe, but have not demonstrated reduced VT recurrence. We sought to describe our experience with the use of Impella for VT RFA in structural heart disease over a 4 year period.
Methods: Retrospective review of 1,236 VT RFAs from May 2011 to August 2015 at our institution. Impella PVAD was used in 67 of these cases; 41 patients had adequate follow-up. Student's t-test and Chi-squared test were used to describe baseline demographics for continuous and categorical variables, respectively. Cox proportional hazards modeling was used to examine factors related to mortality.
Results: Median follow-up time for living (n=35) patients was 152 days (IQR 36-390); median time to mortality (n=6) was 16 days (IQR 11-35). VT recurrence occurred in 11 patients, median time 56 days (IQR 2-206). Chronic obstructive pulmonary disease (HR 5.92, 95% CI 1.08-32.6, p=0.04) and blood urea nitrogen (mg/dL) levels (HR 1.04, 95% CI 1.01-1.07, p=0.02) were both linked with mortality. Femoral vascular complications occurred in 4.9% of patients, requiring repair by vascular surgery.
Conclusions: VT recurrence was only seen in 27% of patients, despite being a sick population. Periprocedural complications were relatively low (5%) and limited to femoral vascular injury (no stroke, MI, valve or aortic injury). The use of Impella is generally safe and may help critically ill patients survive VT ablation and improve outcomes.

Baseline Demographics Stratified by Mortality (% for categorical variables, mean/SD for continuous)

	Alive (n=35)	Deceased (n=6)	p-value
Male	94%	100%	0.55
Caucasian	63%	67%	0.73
Diabetes	29%	25%	0.88
Peripheral Vascular Disease	14%	0%	0.42
Hypertension	66%	40%	0.27
Hyperlipidemia	70%	60%	0.66
Chronic Obstructive Pulmonary Disease	21%	67%	0.03
Creatinine (mg/dL)	1.35 (0.52)	1.26 (0.38)	0.73
Blood Urea Nitrogen (mg/dL)	21.6 (9.06)	41.4 (27.5)	0.003

AB21-03

CRYOBALLOON ABLATION OF PULMONARY VEINS: GANGLIONIC PLEXI MODIFICATION AND AF RECURRENCE

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Introduction: Cryoballoon ablation (CA) of pulmonary veins is an effective treatment for atrial fibrillation (AF). The effect of CA on ganglionic plexi (GP) is unknown. We have observed significant persistent decrease in sinus cycle length (SCL) with CA of right pulmonary veins, likely resulting from ablation of anterior right GP and vagal modulation. The aim of our study is to assess the incidence of GP modification and its relation to AF recurrence.
Methods: Consecutive patients with AF undergoing CA were incuded. Resting HR at baseline, 1 day and 2 months post CA were recorded. Change in sinus cycle length (SCL) during each PV ablation was recorded. Acute and sustained decrease in sinus cycle length by >200 ms during PV ablation was considered a positive vagal modulation (VM). AF recurrence during f/u was documented.
Results: A total of 100 patients (age 64±12, male 69%, paroxysmal AF 92%, HTN 70%, DM 15%, CAD 14%) underwent PV isolation with CA. Compared to baseline HR of 61±10 bpm, there was significant increase in HR at 1 day to 70±9 bpm and at 2 months post CA to 69±10 bpm (P<0.001). SCL decreased from 1165±156 ms at baseline to 880±143 ms post CA (P200ms) was noted in 60% of pts. At a mean f/u of 19±11 months, 74% of pts were AF-free, off AARx following a single procedure . AF recurrence was significantly lower in patients with VM (18%) compared to patients without VM (37%, P<0.05).
Conclusions: During CA, acute decrease in SCL by >200 ms, as a surrogate marker for vagal modulation occurred in 60% of pts. Positive VM was associated with significant decrease in AF recurrence.

	Vagal Modulation +ve (N = 60)	Vagal Modulation −ve (N = 40)	P value
Age	63±11	64±10	NS
Female	27%	36%	NS
HTN	70%	71%	NS
DM	12%	17%	NS
CAD	12%	17%	NS
LA size, mm	42±6	44±6	NS
LVEF, %	53±8	55±5	NS
Heart Rate- Baseline, bpm	61±9	63±10	NS
HR, 1 day	71±10	67±8	0.03
HR, 2 month	70±9	66±11	0.04
SCL, pre	1177±156 ms	1142±149 ms	0.5
SCL, post	833±114 ms	951±153 ms	<0.001
AF recurrence	18%	37%	0.01

AB21-04

RYR2 GENE: DE NOVO VARIANT FREQUENCY, SUDDEN CARDIAC ARREST, & IMPLICATIONS FOR GENETIC COUNSELING

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Introduction: The proportion of de novo (DN) variants in genes is often unknown, which leads to complexities in classifying variants, understanding pathogenicity, and estimating recurrence risks. Although accurate data are not available, the prevalence of DN variants in the RYR2 gene is predicted to be high (up to 40%) (PMID: 20301466).

Methods: Retrospective review of results obtained at our clinical laboratory was performed for targeted familial testing of previously reported RYR2 variants (pathogenic, likely pathogenic, and uncertain significance) to determine the DN frequency.
Results: The cohort included 136 families with 142 informative RYR2 variants. Fifty-two variants occurred DN (37% DN rate). In one family with an apparently DN variant, there was evidence of gonadal mosaicism. More DN variants (42/52; 81.8%) were classified as pathogenic or likely pathogenic compared to 30/90 (33.3%) inherited variants. Sudden cardiac death or arrest (SCD/SCA) was reported in association with 26/90 (29%) inherited RYR2 variants compared to 25/52 (48%) of the DN RYR2 variants. Furthermore, a minority (36/90; 40%) of the inherited variants occurred in a hot-spot (HS) domain whereas the majority (45/52; 87%) of DN variants occurred in a HS domain.
Conclusions: These data provide support for the high frequency of DN variants in the RYR2 gene. DN RYR2 variants confer an approximately 20% greater risk of SCD/SCA compared to inherited RYR2 variants. Correspondingly, DN variants were significantly more likely to be classified as pathogenic or likely pathogenic and are more than two times as likely to occur in a HS. For novel sequence variants, parental testing to establish a DN occurrence has tremendous value for variant classification and determining clinical relevance. In cases of DN RYR2 variants the possibility of non-paternity or gonadal mosaism exists. In apparently DN cases, families should be counseled that siblings of the proband have a small risk of inheriting the variant due to the possibility of gonadal mosaicism. Parental testing is a powerful tool that can provide vital insight regarding pathogenicity of variants, risk for SCD/SCA, and recurrence risk.

AB21-05

PREVENTION AND REGRESSIVE EFFECT OF WEIGHT LOSS AND RISK FACTOR MODIFICATION ON ATRIAL FIBRILLATION (REVERSE-AF)

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Introduction: Atrial Fibrillation (AF) is a progressive disease. The LEGACY study demonstrated a dose-response effect of weight reduction on AF. Here, we evaluated the impact of obesity and weight loss on progression of the AF disease.
Methods: Of 1415 consecutive patients with AF, 825 had BMI≥27kg/m2 and were offered weight management. After screening for exclusion criteria, 355 were included in this analysis. Weight-loss was categorized as Group-1 (<3%); Group-2 (3-9%); and Group-3 (≥10%). Change in AF type was determined by clinic review and 7-day Holter monitoring 12 monthly. AF type was categorized as per HRS consensus.
Results: There were no differences in baseline characteristic or follow up duration between the groups. Group-1 demonstrated the most progression: 41% transitioning from paroxysmal to persistent and 1% from persistent to paroxysmal. There was a stepwise improvement in group-2: 32% progressing from paroxysmal to persistent and 17% from persistent to paroxysmal. Group-3 had best outcome: 3% progressing to persistent and 36% had disease regression from persistent to paroxysmal. In addition, there was a decrease in need for ablation with 87% in group-1, 78% in group-2 and 54% in group-1 requiring ablation. There was no difference in number of patients requiring AV node ablation or pacemaker implantation between the 3 groups (p=NS). (See table)
Conclusions: Sustained obesity is associated with progression from paroxysmal to persistent AF. Weight loss regresses AF disease from persistent to paroxysmal. There was a significant improvement in AF burden and maintenance of sinus rhythm, underscoring the pivotal role to treat risk factors and prevent AF.

RESULTS				
	GROUP 1 <3% WL (N=116)	GROUP 2 3-9% WL (N=104)	GROUP 3 ≥10% WL (N=135)	P-Value
Paroxysmal to Persistent	48 (41%)	33 (32%)	4 (3%)	<0.001
Persistent to Paroxysmal	1 (1%)	18 (17%)	49 (36%)	<0.001
No Ablation	16 (13%)	23 (22%)	62 (46%)	0.001
Ablation	100 (87%)	81 (78%)	73 (54%)	0.03
AV Node Ablation	6 (5%)	5 (5%)	5 (4%)	0.9
Pacemaker Implantation	44 (38%)	35 (34%)	36 (27%)	0.08

AB21-06

"AS NEEDED" SHORT-TERM NOVEL ORAL ANTICOAGULANTS FOR INFREQUENT ATRIAL FIBRILLATION EPISODES GUIDED BY DILIGENT PULSE MONITORING

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Introduction: In patients (pts) with atrial fibrillation (AF) and CHA2DS2-VASc score ≥1, oral anticoagulation therapy (OAT) is recommended, however chronic OAT is associated with a well-defined bleeding risk and pts are often reluctant to take long term daily OAT particularly in the setting of good AF control. We describe the outcome in pts in whom we used novel oral anticoagulants (NOAC: rivoraxiban, apixiban, dabigatran) on an "as needed basis" guided by diligent pulse monitoring to detect recurrent AF.
Methods: Since 2011, we selected 100 highly motivated pts with CHA2DS2-VASc score ≥1 capable of checking their pulse manually and/or with a smartphone enabled device (Alivecor) twice daily and with symptoms. All pts had no AF recurrences by at least three weeks of continuous ECG monitoring and skill and compliance with pulse assessment confirmed. All were provided with a NOAC with instructions to start if suspected or confirmed AF episode ongoing for > 1-2 hours. Duration of NOAC use after restart was based on duration of episode and/or continued paroxysms and discussion with provider (typically a minimum of one week for episode <one day), and pts with frequent AF recurrences were transitioned to continuous daily OAT.
Results: Of the 100 pts (81% male, age 64 ± 8 years old), 84% had AF ablation and the remainder were being treated with drug therapy for AF. All pts utilized pulse assessment and 9 (9%) utilized Alivecor or other smartphone application in addition to pulse taking to confirm the absence of AF. Three patients (3%) had implanted devices capable of quantifying AF episodes as quality control check. The median CHA2DS2-VASc was 2 (range 1-5). The mean left atrial size was 4.1 ± 0.6 cm. During

an average follow-up of 18 ± 14 months (total 150 pt - years), 26 pts (26%) started NOAC at least once for detected AF episode. Six pts (6%) transitioned back to chronic OAT for recurrent AF episodes. There were no thromboembolic events (stroke/TIA) and only 1 mild bleeding event (epistaxis) requiring medical attention.
Conclusions: The use of NOACs on an "as needed basis" when AF is detected with diligent pulse monitoring maybe an effective and safe way to lower patients' overall risk of stroke without increased bleeding in motivated patients with infrequent AF after ablation or drug therapy.

ABSTRACT AB22: Molecular Regulation of Ion Channels

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB22-01

ADRENERGIC-RELATED BI-DIRECTIONAL VENTRICULAR TACHYCARDIA IN A CARDIAC-SPECIFIC R67Q-KCNJ2 MUTANT MOUSE

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Introduction: KCNJ2 mutations, are associated with Anderson-Tawil Syndrome (ATS)/Long QT 7 (LQT7), Short QT Syndrome 3 (SQTS3) and have been implicated in catecholaminergic polymorphic ventricular tachycardia (CPVT3). We previously reported KCNJ2 mutation R67Q, from a patient with adrenergic-induced polymorphic VT (PMVT) and bidirectional ventricular ectopy. R67Q co-expressed with wild-type (WT) KCNJ2 in a heterologous expression system demonstrated a lack of IK1 increase following adrenergic stimulation compared to WT KCNJ2 and R67Q demonstrated decreased rectification index and sensitivity to calcium. However the underlying cellular arrhythmia mechanisms remain unclear. A cardiac-specific R67Q "knock-in" mouse was generated to determine the cellular mechanism and in vivo phenotype.
Methods: Anaesthetised 8-10 week old WT (Cre+/R67Q-/-) and R67Q (Cre+/R67Q+/-) heterozygous mice were studied with continuous ECG measurements, at baseline, and following injection of intraperitoneal (IP) epinephrine (2mg/Kg) and caffeine (120mg/Kg). Right ventricular myocytes were isolated from WT and R67Q heterozygous mice for calcium transient measurements, at baseline, and following isoproterenol administration using standard protocols.
Results: At baseline, ECG for Cre+/R67Q-/- and Cre+/R67Q+/- mice showed sinus rhythm with normal intervals. Following IP-injected epinephrine and caffeine, 4/6 heterozygous R67Q mice showed periods of PMVT, bidirectional VT, bigeminy, and premature ventricular contractions (PVCs). In contrast, WT mice showed sinus rhythm and sinus tachycardia. Isolated cardiomyocytes from Cre+/R67Q-/- mice showed a 1:1 response of calcium transients as a result of electrical field stimulation at 1Hz, 2Hz and 4Hz.
Conclusions: Adrenergic stimulation of heterozygous R67Q mice resulted in bidirectional VT and PMVT account for the CVPT-like phenotype. Our further studies will determine if the mechanism depends on altered calcium handling.

AB22-02

THE TWO-PORE K+ CHANNEL TREK-1 REGULATES SINOATRIAL NODE MEMBRANE EXCITABILITY

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Introduction: Two-pore K+ channels have emerged as potential targets to selectively regulate cardiac cell membrane excitability. However, lack of specific inhibitors or relevant animal models has impeded the effort to understand the role two-pore K+ channels in heart and their potential as a therapeutic target. The objective of this study was to determine the role of mechano-sensitive two-pore K+ channel family member TREK-1 in control of cardiac excitability and heart function.
Methods: Cardiac-specific TREK-1 deficient mice (αMHC-Kcnkf/f) were generated to study role of TREK-1 in heart. Electrocardiograms were measured in 2 month-old αMHC-Kcnkf/f and wildtype (WT) animals at baseline and following stress (treadmill exercise then 2 mg/kg epinephrine injection). TREK-1 expression in mouse sinoatrial node (SAN) was analyzed by immunoblotting of detergent soluble lysates from SAN explants. Spontaneous action potentials (AP) and background K+ current were measured in isolated αMHC-Kcnkf/f and WT SAN cells. Mathematical modeling and parametric analysis was performed using an established model of the mammalian central SAN cell AP modified to incorporate a formulation for TREK-1 current.
Results: αMHC-Kcnkf/f animals showed selective loss of TREK-1 from heart but not other tissues (e.g. brain, pancreas) with bradycardia at baseline and frequent episodes of sinus pause following stress compared to WT. αMHC-Kcnk2f/f SAN APs showed increases in spontaneous firing frequency (6.71±0.2 Hz vs 5.10±0.1 Hz, $p<0.001$) and diastolic depolarization rate (184.6±15.5 mV/s vs 136.1±9.4 mV/s, $p<0.05$) without changes in other properties (max diastolic potential, AP amplitude). Background K+ current was significantly reduced in αMHC-Kcnk2f/f SAN cells (3.95±0.24 pA/pF vs. 5.01±0.42 pA/pF, $p<0.05$) consistent with a loss of TREK-1. Computer simulations predict a specific role for TREK-1 current in regulating SAN AP diastolic depolarization rate and spontaneous firing, consistent with experimental measurements.
Conclusions: These findings identify a TREK-1-dependent pathway essential for normal SAN cell excitability that serves as a potential target for selectively regulating SAN cell function.

AB22-03

PKCδ PHOSPHORYLATION AND MITOCHONDRIAL ROS ARE REQUIRED FOR METABOLIC DOWNREGULATION OF CARDIAC NA+ CHANNEL

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Introduction: NADH increases in cardiomyopathy. NADH upregulates mitochondrial reactive oxygen species (mitoROS) and downregulates cardiac Na+ channel (Nav1.5). Nevertheless, the signaling mediators between NADH, mitoROS, and Nav1.5 downregulation are unclear.
Methods: HEK293 cells transfected with human wild type or

mutant (S1503A and S1503D) Nav1.5 channels were used for whole-cell patch clamp recording and single channel recording. Isolated mouse cardiomyocytes were used to monitor mitoROS levels with MitoSOXTM Red.
Results: NADH activated mainly PKCδ by enhancing phospholipase D activity (1.6±0.1-fold of untreated, P<0.01) and increasing diacylglycerol synthesis. Activated PKCδ translocated to mitochondria and upregulated mitoROS (2.8±0.3-fold of untreated, P<0.01) by enhancing the mitochondrial complexes (I, II and IV) activities (1.1- to 1.5-fold of untreated, P<0.01). PKCδ also translocated to the plasma membrane and interacted with Nav1.5 to downregulat Na+ current (INa) by phosphorylating Nav1.5 at S1503 (and possibly other sites). Reduction in INa by activated PKCδ was prevented by mitochondria-targeted antioxidants, suggesting the requirement of mitoROS for INa downregulation. MitoROS-induced downregulation of INa was prevented by mutating the known PKC phosphorylation site S1503 to Ala, indicating the requirement of PKC-dependent channel phosphorylation. Pseudophosphorylation of this site by Asp substitution was, however, insufficient to downregulate Nav1.5 in the absence of mitoROS. At the single channel level, the mechanism of INa reduction by PKCδ appeared to be a decrease of single channel conductance to 47-55%.
Conclusions: NADH-activated PKCδ modulates both mitoROS and Nav1.5. PKCδ elevates mitoROS via enhancing the mitochondrial complexes activities. PKCδ binds directly to Nav1.5, resulting in channel phosphorylation. PKCδ phosphorylation and mitoROS are both required to downregulate Nav1.5. Alteration in single channel conductance explains the observed changes in whole-cell INa. Inhibiting PKCδ or mitoROS may help raise INa in cardiomyopathy.

AB22-04

MOLECULAR INTERACTION SITES BETWEEN KV4.3 AND DPP6: THE BIOCHEMICAL ANATOMY OF IDIOPATHIC VENTRICULAR FIBRILLATION

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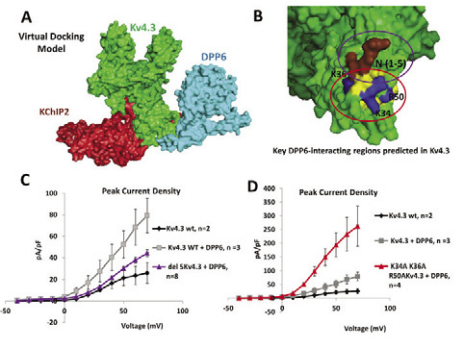
Introduction: The molecular basis of idiopathic ventricular fibrillation (IVF) is poorly understood. We have identified crucial roles of a β subunit, DPP6, in Purkinje fiber Ito and gene variants causing DPP6 gain-of-function in IVF (Xiao et al, Circ Res 112:1310-22, 2013). Little is known about the molecular basis of DPP6 interaction with the Ito α-subunit Kv4.3. Clarifying the structural basis for DPP6-Kv4.3 interaction was the objective of this study.
Methods: We developed a computational model of Kv4.3-DPP6 interaction using AutoDock Vina. Model predictions were verified with WT subunits and engineered mutants expressed in HEK cells, with currents measured by patch clamp 48 hours after transfection.
Results: The model predicts binding between Kv4.3 and its 2 principal β-subunits, KChIP2 and DPP6 (Figure A). The N-terminal region and a positively charged zone on Kv4.3 are identified as key interaction sites with DPP6 (Figure B). WT Kv4.3 showed substantial current enhancement upon co-expression with DPP6 (Figure C), as we have previously reported. Deletion of the Kv4.3 N-terminal region significantly decreased current when co-expressed with DPP6 (Figure C). Neutralization of the 3 predicted-crucial positively charged Kv4.3 amino acids by alanine mutation substantially enhanced the current-increase when Kv4.3 was co-expressed with DPP6 (Figure D).
Conclusions: Kv4.3 interacts with DPP6 via docking involving the N-terminal and crucial positively-charged amino acids. These results provide insights into the biochemical anatomy of IVF and may help to develop effective molecularly-targeted blockers for patients with IVF-inducing DPP6 gain-of-function.



AB22-05

THE ELUCIDATION OF THE CORRECT MECHANISM OF KV7.1 PERTURBATION UNDERLYING A CASE OF R195FS/40- AND D202N-KCNQ1-MEDIATED JERVELL AND LANGE-NIELSEN SYNDROME

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Introduction: Homozygous or compound heterozygous KCNQ1 mutations will cause Jervell and Lange-Nielsen Syndrome (JLNS, severe long QT syndrome plus congenital deafness) as long as the mutations result in profound loss-of-function with < 10% residual Kv7.1 channel activity. The c.604G/A (p.D202N) missense mutation produces a functional channel with mild impairment. Accordingly, JLNS should not be the observed phenotype. However, a JLNS patient, hosting a frameshift mutation and this c.604G/A mutation, was discovered prompting an investigation for alternative pathogenic mechanisms.
Methods: The JLNS patient, father, and mother were recruited and RNA samples were obtained via a Paxgene kit. Four different in silico tools were used (NNSplice, Human Splicing Finder, Max-EntScan, ESEFinder) to understand the potential for c.604G/A (p.D202N) to affect the 5' splice site. Alternative spliced transcripts were identified using primers in exons 1 and 6 and confirmed using Sanger sequencing. Transcript specific primers were used to determine the amounts of each transcript generated in the family members.
Results: The JLNS patient inherited p.R195fs/40 from his father and the c.604G/A (p.D202N) variant from his mother. This c.604G/A variant was predicted to disrupt the 5' splice site by all 4 in silico tools. This disruption resulted in two alternatively spliced transcripts, 1) transcripts skipping exon 3-4 (Δ3-4), which creates an early termination codon and 2) transcripts utilizing an alternative 5' splice site in exon 3 (Alt3) leading to a partially skipping of exon 3 and an early termination codon. However, only the Alt3 transcript was elevated in the c.604G/A-positive individuals, accounting for 46.9% of the KCNQ1 transcripts in c.604G/A-positive individuals.
Conclusions: The impact of c.604G>A on splicing explains the discordance between the clinical phenotype of JLNS and the functional characterization. This highlights that RNA should not be ignored in assessing alternative pathogenic mechanisms as a missense mutation's impact on the biophysical activity of the Kv7.1 channel may not account for the perturbation fully or correctly.

AB22-06

TBX3 CONTROLS THE PACEMAKER FUNCTION OF THE ADULT SINOATRIAL NODE

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Introduction: In the adult, in various conditions (e.g. myocardial infarction, heart failure and pulmonary hypertension) there is sinoatrial node (SAN) dysfunction as well as changes in the expression of Tbx3. Tbx3 is known to play an important role in the embryonic development of the SAN, but the role in the adult is not known. Here, we explore the effects of Tbx3 upregulation in the adult SAN.
Methods: Tbx3 was upregulated in the SAN by crossing CAG-CAT-Tbx3 transgenic mice with heterozygous HCN4-kit transgenic mice: this generates double-transgenic mice conditionally expressing Tbx3 in the SAN. Tbx3 upregulation was induced by injecting tamoxifen (Sigma T5648) IP (40 mg/kg) for 3 days into adult males. The mice were kept for 3 weeks after the last injection.
Results: Quantitative PCR revealed an upregulation of Tbx3 mRNA in the SAN as expected. The ECG measured in the conscious and anaesthetised animal showed significant sinus tachycardia (increase in heart rate of 85±29 and 120±43 beats/min, n=10). SAN pacemaking is determined by the membrane and Ca2+ clocks. The membrane clock may not be responsible for the sinus tachycardia: transcripts of three key ion channels (all involved in the membrane clock) were investigated - HCN1 and Nav1.5 were unchanged, whereas HCN4 was significantly downregulated by 45%. However, the Ca2+ clock may be responsible: transcripts of three key Ca2+ clock components were investigated - RYR2 and NCX1 were unchanged, whereas SERCA2 was significantly upregulated by 152%. We investigated transcripts for a number of transcription factors known to play an important role in the SAN. Mef2c and Tbx18 were unchanged, whereas Rest1 (represses HCN4 expression) was significantly upregulated by 26%, Pitx2 was significantly upregulated by 87% and Nfat4 was significantly upregulated by 730%. A potential Tbx3 binding site on the promoter region of Nfat4 was identified by in silico analysis. Nfat4 is known to upregulate SERCA2 (Prasad and Inesi, AJP, 2011;300:H173-H180).
Conclusions: Tbx3 is able to control SAN pacemaking in the adult possibly by controlling SERCA2 expression via Nfat4.

ABSTRACT PLUS AB23: Genetics of Arrhythmias

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1:30 PM - 3:00 PM

AB23-01

META-ANALYSIS IDENTIFIES TWELVE NOVEL GENETIC LOCI ASSOCIATED WITH ATRIAL FIBRILLATION

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Introduction: Atrial fibrillation (AF) affects more than 33 million people worldwide and increases risk of stroke, heart failure, dementia, and death. Genome-wide association analyses (GWAS) have identified fourteen genetic loci associated with AF. We sought to identify additional genetic loci for AF, by increasing the sample size and the number of variants to be meta-analyzed in the AFGen Consortium.
Methods: We performed genotyping and imputation to the 1000 Genomes reference data in 31 studies in the AFGen Consortium. After rigorous quality control and filtering, each study performed GWAS locally. Summary level statistics from all GWAS were combined in inverse variance weighted meta-analysis, which was performed independently at two study sites for quality control. The presence of expression quantitative trait loci (eQTL) was evaluated through gene expression microarray analyses of 289 atrial appendage samples of European American ethnicity from the Cleveland Clinic AF study.
Results: We included 18,398 individuals with AF and 129,831 referents of European, African-American, Asian, Hispanic, and Brazilian ethnicity in the meta-analysis. We identified twelve novel genetic loci (METTL11B, CEP68, ANXA4, TTN, THRB, SH3PXD2A, SCN10A, PKD2L2, KCNN2, SLC35F1, ASAH1, ADORA2A-AS1) that reached the genome-wide significance level ($P<5x10-8$) and replicated twelve known AF loci. Genetic heterogeneity was observed across ethnicities with regard to effect size and statistical significance. Eight of the genetic loci (CEP68, PKD2L2, ASAH1, MYOZ1/SYNPO2L, CAV1/2, PRRX1, KCNN3, TBX5) identified had significant eQTLs for the gene in closest proximity (FDR<0.05). The genes identified are involved in cardiac structure, regulation of the action potential, and hormonal responses related to AF.
Conclusions: In this study, we identified twelve new genetic loci for AF. Our results provide insight to the molecular background of AF and identify new potential targets for drug discovery.

AB23-02

POST-MORTEM GENETIC TESTING IN YOUNG VICTIMS OF SUDDEN ARRHYTHMIC DEATH SYNDROME

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Introduction: Sudden cardiac death in the young (<40 years) can occur as a result of inherited cardiomyopathy or primary electrical disease. If sudden death is unexplained despite an appropriate autopsy and toxicological assessment the term Sudden Arrhythmic Death Syndrome (SADS) may be used. Establishing a genetic etiology of SADS allows for appropriate screening and management of relatives at risk of SADS. We assessed the yield of postmortem next-generation sequencing (NGS) in young victims of SADS.
Methods: We performed NGS in 189 young sudden cardiac death cases that had structurally normal hearts and negative toxicological analysis at autopsy (i.e. SADS). NGS targeted the coding region of genes associated with primary electrical disease (n=30) and cardiomyopathy (n=64). Variants with a

minor allele frequency >1/1000 in public databases, synonymous variants not located at splice sites and non-truncating variants in TTN were excluded from further analysis. The retained variants were prioritized using a scoring system that combined three in silico pathogenicity prediction tools (SIFT, PolyPhen, MutationTaster), conservation (GERP++) and allele frequency in the general population. The pathogenicity of each variant was further assessed through an extensive literature review. Variants were finally classified as 'pathogenic', 'likely pathogenic' and 'variant of unknown significance'.
Results: NGS was successful in 182 cases. Ten patients (5.5%) were found to harbour a 'pathogenic' variant in genes linked to the primary electrical diseases, whereas one patient had a 'pathogenic' variant in a cardiomyopathy gene. In addition, 20 patients (11%) had 'likely pathogenic' variants in primary electrical disease genes, while 19 patients (10%) had 'likely pathogenic' variants in cardiomyopathy genes. A total of 169 'variants of unknown significance' were found in this cohort. In 63 patients (35%), no rare variant was identified. RYR2 was the gene with the most pathogenic/likely pathogenic variants.
Conclusions: We identified pathogenic/likely pathogenic variants in 27% of SADS cases. These variants represent a starting point for genotype-phenotype studies in the respective families that may allow for presymptomatic diagnosis in a substantial number of families.

AB23-03

WHOLE EXOME SEQUENCING IN SUDDEN INFANT DEATH SYNDROME

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Introduction: Sudden Infant Death Syndrome (SIDS) describes the unexplained sudden death of an infant under 12 months old despite comprehensive clinical and pathological assessment. We hypothesized that whole exome sequencing (WES) will identify putative pathogenic (PP) variants and excess rare variant burden at gene level.
Methods: Genomic DNA from 419 SIDS cases (mean age 2.9 months, 62% male) underwent target enrichment using Agilent SureSelect Human All Exon (+/- UTR) v5 kit and WES on Illumina HiSeq. Reads were aligned to GRCh37 reference genome; variants called with SAMtools and annotated with Annovar. Control allele frequencies were obtained from the ExAC database. Principal component analysis (PCA) was performed to identify North European (NE) ancestry. Case control burden analysis at gene level was performed on NE cases and 729 NE controls, with an initial exome wide analysis followed by a focused 90 gene cardiogenetic disease-susceptibility analysis. A strict ultra rare allele frequency of <0.00005 was used. PP variants were defined as radical variants, all missense variants in KCNQ1, KCNH2, SCN5A and RYR2 and all missense variants with abnormal functional characterization in vitro in the remaining 86 genes. All PP variants were confirmed with Sanger sequencing. Characteristics of SIDS cases were analyzed as potential predictors for hosting a PP variant.
Results: PCA identified 288 cases of NE ancestry. Case control burden analyses did not demonstrate any significant gene association. Overall, 397 ultra rare variants (70.5% of cases) were identified. 55 were classed as PP (12.3% of cases) and the other 342 as variants of unknown significance (VUS). VUS:PP ratio 6.3. Age of 2-4 months and/or supine sleep position had a sensitivity of 0.83 and 90% negative predictive value for a PP variant.
Conclusions: Only a small proportion of SIDS may be due to an underlying cardiac disease. Cases aged 2-4 months and/or found in the supine sleep position may be prioritized for genetic testing. There is however a high yield of ultra rare variants in cardiac genes. The VUS:PP ratio was high representing significant genetic 'noise'. Burden analyses did not detect any significant population level associations suggesting etiological heterogeneity underlying SIDS.

AB23-04

INVESTIGATING THE GENETIC CAUSES OF SUDDEN UNEXPECTED DEATH IN CHILDREN

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Introduction: Sudden unexpected death in the young (SUDY) refers to the non-traumatic sudden unexpected death of a seemingly healthy individual <40 years of age with no identified cause of death at autopsy. Investigation that includes autopsy leads to a diagnosis in most cases; however up to 80% of infant and child cases remain undetermined (autopsy-negative). Genetic and clinical assessment of surviving relatives has shown that nearly 40% of autopsy-negative SUDY cases are due to inherited arrhythmia syndromes (IAS). Genetic testing however is not routinely included in SUDY investigations.
Methods: Autopsy-negative child SUD cases (n=191, aged ≤ 5 years) were selected for our sequencing panel of 70 genes including IAS candidate genes as well as other genes not previously investigated for IAS susceptibility. Libraries were prepared from DNA extracted from post mortem tissue and exonic regions of our genes of interest were captured and amplified using biotinylated DNA probes. The captures were sequenced on a MiSeq platform with 150 bp paired-end reads. After sequencing, the reads were processed and analyzed to identify variants using Geneious software, and annotated using the Oncotator online application. Sequence data were filtered using a minor allele frequency (MAF) threshold of ≤0.01 based on the NHLBI exome sequencing project.
Results: We have uncovered known mutations in IAS candidate genes (e.g. LMNA R644C, CACNA1C G402S) in 16% of our SUD cases. Potentially damaging novel variants were identified in 17%; 10% were in genes not previously investigated for IAS. All novel thin filament gene variants will be functionally characterized in our laboratory. All IAS-associated mutations will be reported to the medical examiner's office, which contacts SUDY-affected families to refer them for clinical assessment.
Conclusions: After further examination of autopsy-negative cases through assessment of genes excluded from IAS genetic testing we propose an expanded set of candidate genes for SUDY. We have successfully identified both novel and known genetic variants that will assist in diagnosis in at least 25% of autopsy-negative child SUD cases and reduce risk of future SUDY in surviving relatives.

AB23-05

NEXT-GENERATION SEQUENCING OF PATIENTS WITH AV NODAL REENTRY TACHYCARDIA IDENTIFIES HIGH PREVALENCE OF FUNCTIONAL MUTATIONS IN SCN5A AND SCN10A

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Introduction: Atrioventricular nodal reentry tachycardia (AVNRT) is the most common form of regular paroxysmal supraventricular tachycardia. This arrhythmia affects women twice as frequently as men, and is often diagnosed in patients below 40 years of age. Familial clustering, early onset of symptoms, and lack of structural anomaly indicate involvement of genetic factors in AVNRT pathophysiology.
We hypothesized that AVNRT patients have a high prevalence of mutations in genes, which are highly expressed in the atrioventricular conduction axis of the heart and potentially involved in arrhythmic diseases.
Methods: Next-generation sequencing of 67 genes was applied to the DNA profile of 97 AVNRT patients and 11 AVNRT family members using HaloPlex Target Enrichment System and selected results were verified using an Illumina next-generation sequencing amplicon-based platform, the TruSeq Custom Amplicon Kit.
Results: In total, we found 99 mutations in 38 genes; 95 missense mutations, two indel mutations, and two splice site mutations. Seventeen of these were novel. Furthermore, we report two AVNRT families with co-segregating mutations. Twenty-nine of 97 AVNRT patients (30%) and three family members to different AVNRT probands had one or more mutations in genes affecting the sodium handling. Twenty-two out of 97 AVNRT patients (23%) had mutations in genes affecting the calcium handling of the heart. We furthermore find a large proportion of mutations in the HCN1-4 genes. Many of the known sodium channel mutations have been functionally characterized. Four out of five SCN5A mutations and two out of two identified SCN10A mutations has been shown to compromise the sodium current.
Conclusions: This indicates that AVNRT might be an electrical arrhythmic disease with abnormal sodium channel function.

ABSTRACT PLUS AB24: Advances in Atrial Fibrillation

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1:30 PM - 3:00 PM

AB24-01

NERVE SPROUTING, SYMPATHETIC HYPERINNERVATION AND INCREASED VULNERABILITY TO ATRIAL FIBRILLATION IN A PORCINE MODEL OF METABOLIC SYNDROME

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Introduction: Previous studies suggested that obesity and metabolic syndrome (MetS) are independent risk factors of atrial fibrillation (AF). However, mechanisms underlying the relation between MetS and AF remain speculative.
Methods: N/A.
Results: In our Lee-Sung porcine model, western diet-induced MetS was established by central obesity, high blood pressure, high serum triglyceride levels, and insulin resistance. We fed Lee-Sung minipigs with western diet (MetS, N=7) or standard diet (Control, N=8) for 6 months. Nerve sprouting (growth associated protein 43, GAP43, positive nerve) and sympathetic innervation (Tyrosine hydroxylase, TH, positive nerve) of left atrium (LA) in MetS group and Control group were determined by immunochemical staining. Density of GAP43- and TH-positive nerves in LA were significantly higher in MetS group than that in the Control group ($p<0.01$). In in-vivo electrophysiological study, the sustained atrial fibrillation was induced in 6/7 of hearts in MetS group and none (0/8) of hearts in Control group. The total atrial fibrillation burden was also significant higher in those hearts with MetS as compared with hearts in Control group (112±150 vs 5.9±7.8 sec/episode; $p<0.01$).
Conclusions: Neural remodeling with atrial nerve sprouting and sympathetic hyperinnervation was associated with increased vulnerability to atrial fibrillation in our Lee-Sung porcine model of MetS.

AB24-02

A NOVEL HUMAN ATRIAL MODEL BASED ON A HIGH RESOLUTION FUNCTIONALLY AND STRUCTURALLY MAPPED INTACT HUMAN HEART TO RESOLVE STRUCTURAL SUBSTRATE OF ATRIAL FIBRILLATION DRIVERS

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Introduction: Structural remodeling of human atria can play a key role in sustaining atrial fibrillation (AF), but lack of quantitative tools and reliable data from human atria impedes the clinical treatment of AF. We aim to develop a 3D computer model of human atria based on high resolution functional and structural mapping of the human atria with history of AF.
Methods: High resolution panoramic epicardial optical mapping of the coronary-perfused explanted human atria (HTN, 63 y.o.

female) was conducted during normal rhythm and sustained AF (> 70 min). Whole atria were imaged with gadolinium enhancement (GE) MRI (9.4T) at a spatial resolution of 170×170×340 µm³ to visualize 3D fibrosis distribution and atrial myofiber orientation with structure tensor analysis. A human atrial computer model was constructed by incorporating these structural and functional imaging data.
Results: Optical mapping identified localized stable AF drivers in the posterior left atrium. Correlation of functional mapping with GE MRI revealed that stable AF drivers were anchored to regions of high fibrosis content and myofiber twists. The computational approach based on human atrial structure and function accurately simulated atrial activation and repolarization during normal rhythm and AF. Importantly, during AF simulation the computer model accurately reproduced the location and activation pattern of the functionally-identified reentrant driver.
Conclusions: The 3D anatomically and functionally human-based computational framework may provide a powerful vehicle for exploring the structure-function substrates underlying AF and develop new efficient patient-specific treatment strategies.

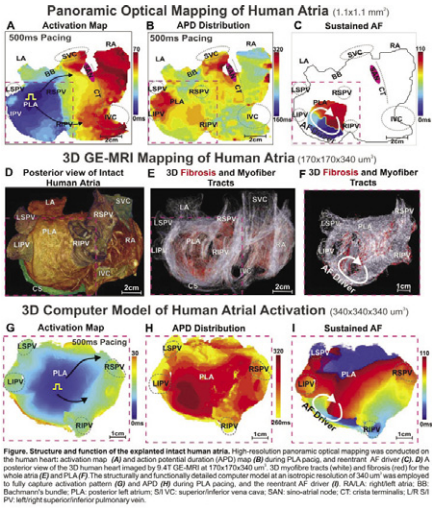

Figure. Structure and function of the explanted intact human atria. High-resolution panoramic optical mapping was conducted on the human heart: activation map *(A)* and action potential duration (APD) map *(B)* during PLA pacig, and reentrant AF driver *(C)*. *(I)* A posterior view of the 3D human heart imaged by 9.4T GE-MRI at 170x170x340 um³. 3D myofibre tracts (white) and fibrosis (red) for the whole atria *(E)* and PLA *(F)*. The structurally and functionally detailed computer model at an isotropic resolution of 340um³ was employed to fully capture activation pattern *(G)* and APD *(H)* during PLA pacing, and the reentrant AF driver *(I)*. RA/LA: right/left atria; BB: Bachmann's bundle; PLA: posterior left atrium; SI VC: superior/inferior vena cava; SAN: sino-atrial node; CT: crista terminalis; L/R SI PV: left/right superior/inferior pulmonary vein.

AB24-03

ANGIOTENSIN IV IS A PROARRHYTHMOGENIC FACTOR IN ATRIAL FIBRILLATION

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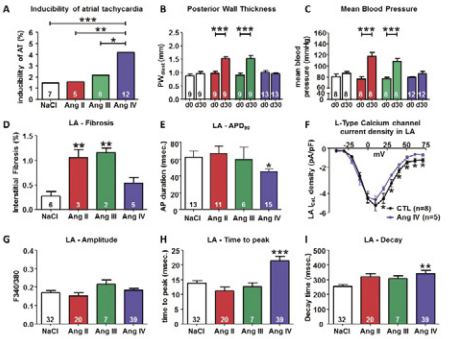
Introduction: Atrial Fibrillation (AF) is the most common arrhythmia worldwide. Genome-wide association studies identified c9orf3 as a risk locus for AF. C9orf3 encodes an aminopeptidase that has been shown to cleave angiotensin III (AngIII) to angiotensin IV (AngIV).
Methods: To evaluate the functional role of AngIV in AF we treated C57BL/6 mice with AngIV for 4 weeks and performed blood pressure measurement, echocardiography, ECG, invasive and cellular EP studies. As controls we treated mice with saline (CTL), angiotensin II (AngII), or angiotensin III (AngIII).
Results: AngIV treatment resulted in significantly increased inducibility of atrial tachycardia (4.2% vs. 1.5% (CTL), 1.6% (AngII), 2.2% (AngIII), Fig.1A). ECG parameters and Na+, K+ levels in plasma were normal among all groups. Evaluation of structural remodeling did not show any significant differences between AngIV treatment and control regarding blood pressure, posterior wall thickness, or LA fibrosis (Fig.1B-D). AngIV treatment shortened the action potential duration (APD) of LA cardiomyocytes isolated from treated mice (Fig.1E) and reduced the current density of the L-type calcium channel (Fig.1F). Calcium transient measurements on these cells showed a significant prolongation of the time to peak and the decay time whereas the amplitude remained unchanged (Fig.1G-I).
Conclusions: In conclusion, AngIV treatment increased AF inducibility without creating a structural substrate. In vitro experiments suggest effects of AngIV on calcium handling. AngIV may therefore be an important mediator of electrical remodeling in AF and could be an interesting target for drug development.



AB24-04

LOW-LEVEL BUT NOT HIGH-LEVEL BARORECEPTOR STIMULATION INHIBITS ATRIAL FIBRILLATION IN A PIG MODEL OF OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is associated with increased occurrence of atrial fibrillation (AF) mainly driven by combined sympatho-vagal hyperactivation during obstructive respiratory events. Low-level baroreceptor stimulation (LL-BRS), at voltages not slowing sinus rate or AV-conduction, has been shown to inhibit AF. The purpose of this study was to investigate the effect of LL-BRS compared to high-level (HL-) BRS on apnea associated AF-inducibility in a pig model of OSA.
Methods: Sixteen pigs received a tracheotomy under general urethane/chloralose anesthesia. The tracheal tube was connected to a negative pressure device to mimick obstructive respiratory events with defined negative thoracic pressure (NTP). Group 1 pigs (n=8) received LL-BRS (80% below that which slowed the sinus rate) for 3 hours and group 2 pigs (n=8) received HL-BRS (slowing sinus rate). Before and at the end of the 3-hour stimulation protocol, three subsequent NTP-maneuvers for 1 minute were performed. Changes in atrial effective refractory period (AERP) and inducibility of AF were determined.
Results: Group 1: 3 hours of LL-BRS resulted in a progressive lengthening in AERP from 150±5 ms to 172±19 ms (p=0.05). After 3 hours of LL-BRS, NTP-induced AERP-shortening was diminished from -51±10 ms before LL-BRS (-34 %) to -22±4 ms at 3 hours of LL-BRS (-13 %) (p<0.01). AF-inducibility during NTP maneuvers decreased from 90% at baseline to 15% after LL-BRS (p<0.01). Group 2: 3 hours of HL-BRS resulted in a rapid shortening in AERP from 150±17 ms to 132±8 ms (p<0.01) and increased AF-inducibility during normal breathing. After 3 hours of HL-BRS, NTP-induced AERP-shortening was increased from -55±7 ms before HL-BRS (-36 %) to -72±11 ms at 3 hours of HL-BRS (-54 %) (p<0.05). NTP-induced changes in blood

gases, intra thoracic pressure changes and blood pressure were not significantly different between the groups.
Conclusions: Carefully dosed LL-BRS suppressed NTP-induced AERP-shortening and AF inducibility. By contrast HL-BRS further perpetuated NTP-induced AERP-shortening and highly increased AF inducibilty. These findings have potential clinical implications and support the use of LL-BRS as a novel therapeutic modality to treat AF in OSA.

AB24-05

TREK-1 (K2P2.1) K+ CHANNEL GENE THERAPY PROVIDES RHYTHM CONTROL IN ATRIAL FIBRILLATION

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Introduction: Atrial fibrillation is associated with electrical and structural changes of atrial cardiomyocytes, which include dysregulation of potassium channels and fibrosis. We hypothesized that downregulation of atrial TREK-1 (K2P2.1) K+ channel contributes to AF pathophysiology and that normalization of its expression would provide rhythm control.
Methods: Persistent AF was induced in domestic pigs by atrial burst pacing. The animals underwent electrophysiological and echocardiographic examination on day 1 and prior to euthanization (day 14). Right atrial tissue samples were obtained from pigs with gene transfer (AF: n=5; sinusrhythm (SR): n=5) and compared to sham-treated controls (AF: n=5; SR: n=5). TREK-1 remodeling was studied by Western Blot and RT-qPCR. Evaluation of fibrosis, inflammation and apoptosis were performed by Masson-, HE- and TUNEL-stain. Human tissue samples were analyzed by quantitative real time PCR.
Results: Atrial TREK-1 mRNA levels were reduced in patients with chronic AF by 63% (left atrium) and 76% (right atrium) compared to SR controls. These findings could also be observed in a porcine model of atrial tachypacing-induced AF. TREK-1 mRNA (-66%) and protein (-61%) were suppressed in AF animals at 14-day follow-up compared to SR controls. Downregulation of repolarizing TREK-1 channels was associated with prolongation of atrial effective refractory periods (AERP300 baseline: 167 ms; AERP300 14d: 273 ms). Gene therapeutic treatment achieved a SR prevalence of 62% during follow-up, compared to 35% in the untreated AF group. Gene transfer increased TREK-1 protein levels effectively and AERP300 14d was shortened to 210 ms in AF pigs. Reduction of left ventricular ejection fraction (LVEF) in untreated AF animals from 81% at baseline to 51% upon follow-up was attenuated by antiarrhythmic Ad-TREK-1 treatment (LVEF baseline: 81%; LVEF 14d: 72%). Ad-TREK-1 application was not associated with local inflammatory response, fibrosis or apoptosis.
Conclusions: In conclusion, restoration of SR by Ad-TREK-1 transfer indicates mechanistic significance of TREK-1 downregulation in AF. Functional correction of ionic remodeling through TREK-1 gene therapy represents a novel paradigm to optimize and specify AF management.

ABSTRACT AB25:
Lessons Learned for Ongoing ICD Registries

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1:30 PM - 3:00 PM

AB25-01

THE ICD SPORTS REGISTRY: LONG-TERM FOLLOW UP

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Introduction: The ICD Sports Registry showed no sports-related deaths, arrests, or injuries over two years of follow-up. Whether sports participation for longer periods is safe is unknown.
Methods: Athletes with ICDs (N=440; age 10-60 years) participating in competitive (N=393) or dangerous (N=47) sports were recruited by sites (N=270 subjects) or through internet patient advocacy groups (N=170). Sports-related and clinical data were obtained by phone interview and medical records, with follow-up phone calls every 6 months. ICD shock data and clinical details of lead malfunction were adjudicated.
Results: Median age was 40 years, 37% female, 44% had a pre-ICD history of VT/VF. Most common diagnoses were LQTS, (N=87), HCM (N=75), and ARVC (N=55). Running, basketball, and soccer were the most common sports. Over a median FU 44 months, (iqr 30-48), (totaling 1,456 patient-years follow-up,) 33% of athletes received shocks, 12% during competition or practice (table). There were no occurrences of either primary endpoint: 1) death or resuscitated arrest, or 2) arrhythmia- or shock-related injury, during sports. Freedom from lead malfunction was 95% at 5 years (from implant) and 85% at 10 years. There were 11 VT/VF episodes for which multiple shocks were received: 2 at rest, 4 competition/practice, 5 other physical activity, although all were ultimately terminated by the device.
Conclusions: While 12% of athletes received a shock during competition/practice, there were no serious adverse sequelae. These data continue to support the recent change in consensus recommendations to allow individualized and shared decision making for athletes with ICDs wishing to continue competitive sports.

Shock events. Values refer to total events/unique individuals. %s refer to % of study population				
	Competition	Physical Activity	Other	Total
VT	30/22	15/11	19/13	65/54 (12%)
VF	12/10	9/8	14/9	35/27 (6%)
VT/VF storm	4/4	3/3	2/2	9/9 (3%)
AF/Other SVT	10/8	18/14	5/5	33/27 (6%)
Sinus tachycardia	8/7	4/3	1/1	13/11 (3%)
AF/SVT/ST storm	0	3/2	0	3/2 (<1%)
T-wave oversensing	2/2	3/2	3/3	8/7 (2%)
Noise	1/1	7/7	11/10	19/18 (4%)
Total	67/54 (12%)	62/51 (12%)	55/43 (10%)	184/148 (33%)

AB25-02

ELECTRA (EUROPEAN LEAD EXTRACTION CONTROLLED) REGISTRY: LONG-TERM OUTCOMES ON TRANSVENOUS LEAD EXTRACTION IN EUROPE

Maria Grazia Bongiorni, MD, Charles Kennergren, MD, PHD, FHRS, Christian Butter, MD, Jean-Claude Deharo, MD, Andrzej Kutarski, MD, PhD, Christopher A. Rinaldi, MD, Simone Lorenzo Romano, MD, Aldo P. Maggioni, MD, Carina B. Blomstrom Lundqvist, MD, PhD, Angelo Auricchio, MD, PhD and Karl-Heinz Kuck, MD, FHRS. University Hospital of Pisa, Pisa, Italy, Sahlgrenska University Hospital, Gothenburg, Sweden, Herzzentrum Brandenburg in Bernau/Berlin, Bernau / Berlin, Germany, Hôpital La Timone, Marseille, France, Medical University of Lublin, Lublin, Poland, St. Thomas's Hospital, London, United Kingdom, ESC, EORP Department, Sophie Antipolis, France, Uppsala University - Uppsala University Hospital, S-75185 Uppsala, Sweden, Fondazione Cardiocentro Ticino, Lugano, Switzerland, Asklepios Klinik St. Georg, Hamburg, Germany

Introduction: The rate of cardiac rhythm device implantations and the subsequent complications are increasing, leading to a parallel growth of Transvenous Lead Extraction (TLE) procedures. This registry is the first multi-national, multicentre, prospective, registry of consecutive patients undergoing TLE in European countries.
Methods: Data from 76 centres in 19 countries were collected using a web-based system. The primary objective was to evaluate the acute and long term safety of TLE; secondary objectives included the description of patients characteristics, type of leads, indications for TLE, extraction techniques, success rate of TLE and the comparison of outcomes between low and high volume centres defined on the basis of their volume of activity in the registry. Patient recruitment started on November 2012 and ended on May 31 2014. Patients are followed up to 1 year and follow up is expected to be completed at the end of December 2015.
Results: A total of 3555 consecutive patients were enrolled, undergoing extraction of 6493 leads with an average dwell time (±SD) of 6.4±5.4 years. Leads (53.4% with active and 46.6% with passive fixation) were extracted from the right atrium (34.2%), right ventricle (55.2%), coronary sinus (8.4%) and other locations (2.2%). Indications were infection in 52.7% of patients with 47.3% having a non-infectious indication. Complete radiological success was 95.7%, partial radiological success 2.8%, and radiological failure was 1.5%. Major and minor complications were 2.7% and 5.1%. In-hospital mortality was 1.4%. High-volume centres had fewer major and minor complications compared to low volume centres (major 2.4% vs 4.1% p=0.01, minor 4.5% Vs 7.8% p=0.0008). The incidence of clinical failed TLE procedures, as well as long-term complications (12 months follow-up) will be presented.
Conclusions: In this large study, success rates were very high both in high and low-volume centres. Major and minor complications were low compared with previous major studies, especially in high-volume centres. These results, including pending 12 month follow-up data, will be useful to improve the quality of care in lead extraction.

AB25-04

SEATTLE HEART FAILURE MODEL RISK IS STRONGLY ASSOCIATED WITH SURVIVAL AFTER ICD AND CRT-D IMPLANTATION IN THE NCDR ICD REGISTRY

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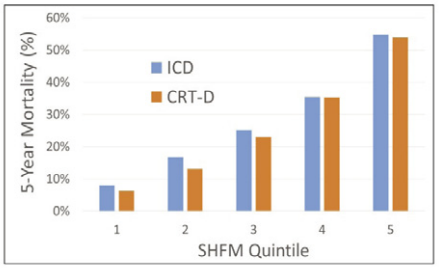
Introduction: Risk models are greatly needed for implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy defibrillators (CRT-D) in order to improve cost effectiveness and patient outcomes. The Seattle Heart Failure Model (SHFM) performs well in clinical trial cohorts but has not been evaluated in a large real-world ICD registry.
Methods: The SHFM was calculated for patients in the NCDR ICD Registry in 2006-2009 with new primary prevention ICD and CRT-D implants. 5-year survival was determined using the Social Security Death Index. Differences in 5-year survival after implantation were determined for SFHM quintiles, and Cox proportional hazards regression was also performed.
Results: The 66,581 patients in the cohort (age 68.4±11.7 years, 26.4% female, 66.0% with ischemic cardiomyopathy, LVEF 25.9±8.1%, serum creatinine 1.3±0.62 mg/dl) included n=36,146 with standard ICDs and n=30,435 with CRT-D. The SHFM conveyed a graded increase in mortality rates in both ICD and CRT-D patients, with an increase in 5-year mortality from 8.0 to 54.7% in SHFM quintiles 1 v. 5 in ICD patients, and from 6.3 to 53.9% in CRT-D patients (p<0.0001). In a Cox model, increasing SFHM as a continuous variable was also strongly associated with survival (p<0.0001).
Conclusions: SHFM risk is strongly associated with survival after ICD or CRT-D implantation in the large NCDR ICD registry. Comparison with a propensity-matched cohort with heart failure but without ICDs is indicated and underway to confirm the different improvements in survival associated with ICDs in SHFM groups. The SHFM is effective for predicting real-world survival rates of patients after ICDs.



AB25-05

DOWNGRADING FROM CRT-D TO CRT-P AT THE TIME OF BATTERY DEPLETION: PRELIMINARY RESULTS FROM DECODE REGISTRY TRIAL

Maria Lucia Narducci, MD, Matteo Santamaria, MD, Domenico Potenza, MD, Francesco Zanon, MD, FHRS, Michele Manzo, MD, Giuseppe Stabile, MD, Matteo Iori, MD, Ernesto Ammendola, MD, Valerio Zacà, MD, Massimo Zoni Berisso, MD, Attilio Pierantozzi, MD, Alberto Bandini, MD, Leonardo Calò, MD, Paolo Sabbatani, MD, Mauro Zennaro, MD, Maria Selina Argnani, MD, Maurizio Malacrida, MS and Mauro Biffi, MD. Catholic University of the Sacred Heart - Insitute of Cardiology, Rome, Italy, Catholic Univ of the Sacred Hea Cardiovascular Dept, Campobasso, Italy, Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG), Italy, Ospedale S. Maria Della Misericordia, Rovigo, Italy, A.O. Ruggi D'Aragona, Salerno, Italy, Clinica Mediterranea, Napoli, Italy, Hospital S. Maria Nuova, Reggio Emilia, Italy, Second University of Naples, A.O. Monaldi, Napoli, Italy, Hospital S. Maria alle Scotte, Siena, Italy, Hospital Padre Micone, Sestri Ponente (GE), Italy, Ospedali Riuniti, Pesaro, Italy, Ospedale Morgagni Pierantoni, Forlì, Italy, Policlinico Casilino, Roma, Italy, Cardiology Department, Bufalini Hospital, Cesena, Italy, Hospital S. Agostino, Baggiovara (MO), Italy, Hospital S. Maria delle Croci, Ravenna, Italy, Boston Scientific Italia, Milano, Italy, Institute of Cardiology, University of Bologna, Policlinico S.Orsola-Malpighi, Bologna, Italy

Introduction: Data from Madit-CRT showed that CRT-defibrillator (CRTD) patients (pts) who achieve ejection fraction (LVEF) normalization (>50%) have very low absolute and relative risk of Ventricular Tachyarrhythmias (VTAs) and a favorable clinical course within 2.2 years of follow-up. These pts could be considered for downgrade to CRT-pacemaker (CRTP) at the time of battery depletion if no VTAs have occurred.
Methods: The DECODE Registry enrolled consecutive pts who underwent CRTD replacement from 2013 to 2015 in 36 Italian centers. At the time of replacement, clinical and echocardiographic findings were assessed and the number of appropriate therapies delivered by the replaced device or pre-implantation history of VTAs was retrieved. The occurrence of appropriate ICD therapies was measured during follow-up.
Results: A total of 313 pts with complete data were considered for this analysis (age 70±10 years, male gender 73%, ischemic etiology 47%, NYHA class I/II at replacement 64%, mean LVEF 35±10%). 197 (63%) pts had LVEF ≤35% whereas 33 (11%) pts achieved LVEF normalization. 115 (37%) pts received ≥1 appropriate ICD therapies prior to replacement and 24 (8%) had secondary prevention indication to ICD at the time of first implantation. Overall, clinical indication to ICD did not persist at replacement in 70 (22%) pts. During a median follow up of 365 [25th-75th: 315-415] days, 31 (10%) pts received an appropriate therapy (17% of pts with and 6% of pts without a previous appropriate ICD therapy, p=0.0015). At multivariable analysis, an appropriate therapy prior to device replacement (OR 3.46, 95%CI 1.44 to 8.28; p=0.005) and low glomerular filtration rate (OR 1.01, 95%CI 1.00 to 1.03; p=0.038) were independent predictors of appropriate ICD therapy within 12 months follow-up. Both LVEF normalization and the persistence of ICD indication were not associated to the occurrence of VTAs after ICD replacement.
Conclusions: Clinical indication to ICD does not persist in approximately 22% of CRTD pts who outlive their first device and about 11% of pts achieved LVEF normalization. Although these pts seem at lower risk and could be considered for downgrading to CRTP, our post-replacement data showed a non-negligible risk of VTAs within 12 months follow-up.

AB25-06

CONTRASTING PROFILES OF USA VERSUS OUTSIDE OF USA CRT RECIPIENTS: INSIGHTS FROM THE INTERNATIONAL ADVANCE CRT REGISTRY

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Introduction: Cardiac resynchronization therapy (CRT) is used worldwide to treat heart failure (HF) patients (pts). However, little is known regarding differences in its application to USA vs. outside USA (OUS) pts.
Methods: ADVANCE-CRT aims to elucidate CRT non-responders' management in clinical practice worldwide (41 USA and 26 OUS centers). Enrollment data were analysed to determine whether baseline differences existed between 1105 USA and 362 OUS pts. (n: India 198, China 44, Korea 35, Japan 33, Columbia 25, Brazil 19, and Argentina 8).
Results: USA and OUS CRT pts were similar in gender distribution (68% male), and percentage of subjects with NYHA Class III HF, diabetes, and pharmacologic antiarrhythmic treatment (21%). OUS pts were younger (62.9±11.1 vs. 69.5± 11.2 years;p<.0001), included a smaller percentage of pts on guidelines directed medical therapy, but were more likely to have LBBB, QRS greater than 150 ms, non-ischemic cardiomyopathy, and poorer LV function. In contrast, USA pts were more obese, more likely to have milder HF, AF and a smoking history. In USA pts, the left ventricular (LV) lead was more likely to be a quadripolar implanted in the lateral location (p<.0001). In contrast, in OUS pts, LV leads tended to be bipolar and sited posterolaterally (p<.0001). CRT defibrillator was used more than CRT pacemaker in USA and OUS, but the proportion was higher in USA (p<.0001).
Conclusions: Despite a common set of CRT practice guidelines, the USA and OUS populations significantly differ in terms of baseline characteristics and implanted CRT system.

Demographic Table

Variable		All	US	OUS	p-value
NYHA (%)	I - II	365 (24.9%)	307 (27.8%)	58 (16.1%)	<.0001
	III - IV	1098 (75.1%)	795 (72.2%)	303 (65.9%)	
LVEF (std)		29.2 (11.2)	30.3 (11.8)	25.7 (8.2)	<.0001
Ischemic Cardiomyopathy (%)		574 (40.0%)	519 (47.4%)	55 (16.1%)	<.0001
Cardiac Risk Factors	Atrial Arrhythmia	552 (38.5%)	523 (47.8%)	29 (8.5%)	<.0001
	Diabetes	553 (38.5%)	431 (39.4%)	122 (35.8%)	0.23
	Cigarettes Smoking	665 (46.3%)	592 (54.1%)	73 (21.4%)	<.0001
	Hypertension	1073 (74.8%)	911 (83.3%)	162 (47.5%)	<.0001
	BMI >= 30	505 (34.5%)	464 (42.1%)	41 (11.4%)	<.0001
ECG Findings	QRS > 150	724 (53.0%)	491 (48.3%)	233 (66.6%)	<.0001
	LBBB	710 (48.7%)	433 (39.4%)	277 (77.4%)	<.0001
Medications (%)	ACEI or ARBS or Both	1047 (71.4%)	804 (72.8%)	243 (67.1%)	0.04
	Beta Blockers	1206 (82.2%)	935 (84.6%)	271 (74.9%)	<.0001
LV Lead Type (%)	Quadripolar	1083 (74.7%)	931 (85.4%)	152 (42.5%)	<.0001
Lead Implant Location (%)	Anterior Lateral	206 (14.3%)	170 (15.6%)	36 (10.3%)	<.0001
	Lateral	629 (43.4%)	542 (49.5%)	87 (24.6%)	
	Posterior Lateral	491 (34.0%)	288 (26.3%)	203 (58.0%)	
	Others	122 (8.4%)	94 (8.6%)	28 (7.8%)	
Device Type (%)	CRT-D	1096 (74.7%)	860 (77.8%)	236 (65.2%)	<.0001
	CRT-P	371 (25.4%)	245 (22.2%)	126 (35.1%)	

ABSTRACT PLUS AB26:
Pacing and Defibrillation: the World is Changing!

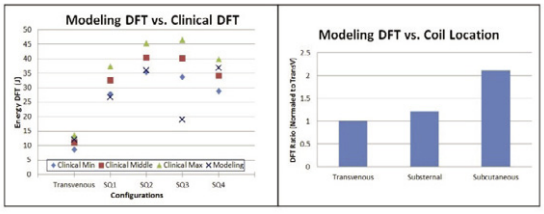
Friday, May 6, 2016
1:30 PM - 3:00 PM

AB26-01

MODELING OF NOVEL SUBSTERNAL DEFIBRILLATION COIL ELECTRODE LOCATION SHOWS SIGNIFICANT REDUCTION IN DEFIBRILLATION THRESHOLD COMPARED TO A SUBCUTANEOUS ICD SYSTEM

Peter Zhang, PhD, Yanina Grinberg, MASc, Vladimir P. Nikolski, PhD, Paul Degroot, MASc, Mark Marshall, MASc, Narendra Simha, PhD and Wei Gan, PhD. Medtronic, Mounds View, MN, Medtronic, Inc., Minneapolis, MN

Introduction: A subcutaneous (SQ) ICD has emerged as an alternative to transvenous (TV) ICD, but with electrodes outside the chest wall they require higher energy to achieve effective defibrillation. A novel extravascular ICD concept which places a coil electrode in the substernal space between sternum and heart may significantly reduce defibrillation thresholds (DFTs) as compared with the present SQ ICD, allowing for smaller device size and greater patient comfort. To verify this assertion, we created human thorax Finite Element Analysis (FEA) models and computed DFTs for various electrode configurations including five configurations from a published SQ ICD clinical trial.
Methods: A human thorax model was created based on a CT scan and scaled to represent a median size adult. The Critical Mass Assumption was used to calculate DFTs. Model predictions were compared for a coil placed either in the substernal space at the midline, subcutaneously adjacent to the sternum, and in the RV apex. An ICD Can was modeled on mid-axillary line at the level of the heart for extravascular ICD leads and in a pectoral location for the RV lead.
Results: In the figure below, the left panel shows that model DFTs match published clinical DFT data; the right panel shows the DFT for all 3 locations. The substernal coil DFT is significantly lower than for the SQ coil and is about 22% higher than DFT for the RV coil.
Conclusions: Results show that a novel substernal coil electrode may significantly reduce defibrillation energy required for an extravascular ICD.



AB26-02

NOVEL EXTRAVASCULAR DEFIBRILLATION CONFIGURATION WITH A COIL IN THE SUBSTERNAL SPACE

Joseph YS Chan, MD, Jacek Lelakowski, MD, PhD, Francis D. Murgatroyd, MD, Lucas V. Boersma, MD, PhD, Jian Cao, PhD, Vladimir Nikolski, PhD, Griet Wouters, MSc and Mark CS. Hall, MD, FRCP. Prince of Wales Hospital, Hong Kong, Hong Kong, The John Paul II Hospital, Krakow, Poland, King's College Hospital, London, United Kingdom, St. Antonius Hospital, Nieuwegein, Netherlands, Medtronic Inc., Mounds View, MN, Medtronic Inc., Maastricht, Netherlands, Liverpool Heart and Chest Hospital, Liverpool, United Kingdom

Introduction: Subcutaneous (SQ) ICDs are regarded as alternatives to transvenous (TV) ICDs in certain patients (pts). However, a substantially higher shock energy up to 80J may be required primarily because both the parasternal shock coil and lateral ICD can are outside the rib cage. Proposed is a new defibrillation method of placing the shock coil into the space immediately behind the sternum. This study assessed the defibrillation efficacy of the substernal-lateral electrode configuration.
Methods: This prospective, non-randomized, feasibility study was conducted in pts about to undergo midline sternotomy or implant of a SQ or TV ICD. A tunneling tool (6996T, Medtronic) was used to insert an 8 cm coil defibrillation lead (6937, Medtronic) behind the sternum using a percutaneous sub-xiphoid approach under fluoroscopic guidance. A skin patch electrode (Fast Patch Plus, Physio Control) was placed on the left thorax at the 4th to 5th intercostal space. After ventricular fibrillation (VF) induction, a single 35J shock was delivered between the substernal coil and the left lateral patch using an external TV ICD (Protecta, Medtronic), with external rescue shock if needed.
Results: Sixteen pts (12 males, 4 females; mean age: 61.6 ± 11.8 years; BMI: 25.6 ± 3.3; LVEF: 47 ± 18%) were enrolled at 5 sites in Europe and Hong Kong. Ten studies preceded sternotomy (2 coronary bypass grafting; 7 valve repair/replacement; 1 aortic aneurysm repair) and 6 preceded ICD implants (5 SQ and 1 TV). All were under general anesthesia except 4 out of 5 SQ ICD pts which were under conscious sedation. Mean lead placement time was 11.1 ± 6.6 minutes. Of the 14 pts with successfully induced VF episodes, 13 pts (92.9%) had successful defibrillation at 35J. The one failure was associated with high and lateral shock coil placement, and one external rescue shock was successful. Mean VF duration was 18.4 ± 5.6 seconds with shock impedance of 98.1 ± 19.3 ohms. Of the 11 pts with coil-patch electrograms, the average R-wave amplitude during normal sinus rhythm was 3.0 ± 1.4 mV.
Conclusions: These preliminary data demonstrate that substernal defibrillation is feasible and that successful defibrillation can be achieved with the shock energy available in current TV ICDs. This may open new alternatives to TV ICD therapy.

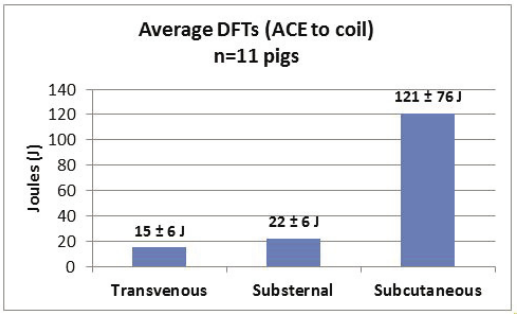
AB26-03

COMPARISON OF DEFIBRILLATION THRESHOLDS IN SWINE FOR TRANSVENOUS, SUBCUTANEOUS AND SUBSTERNAL ELECTRODE CONFIGURATIONS

Amy E. Thompson, MS, Vladimir P. Nikolski, PhD, Melissa G. Christie, MS, Jian Cao, PhD and Paul Degroot, MS. Medtronic, Mounds View, MN, Medtronic, Inc., Minneapolis, MN, Medtronic, Inc., Mounds View, MN

Introduction: Transvenous (TV) ICD systems represent the device-based standard of care for treatment of arrhythmia, yet TV lead implantation is often not possible or desired. Subcutaneous (SQ) ICDs have emerged as a non-TV option, but energy requirements for defibrillation through the chest wall have resulted in larger, heavier SQ ICDs with high defibrillation thresholds (DFTs). Described here are the results of preclinical animal research evaluating the DFT of a novel substernal-lateral electrode vector, as compared to both TV and SQ DFTs.
Methods: Each animal was implanted with three leads. A 5.7 cm coil was implanted in the right ventricle via jugular access, an 8 cm coil was tunneled SQ and positioned parasternally (right side) and an 8 cm coil was introduced into the substernal (SS)

space at or adjacent the sternal midline via minimally invasive subxiphoid access. An active can emulator (ACE) was placed in a pocket on the left lateral thorax at the level of the heart. DFT testing was performed using a step-up, step-down DFT search protocol, with DFTs calculated via logistic regression.
Results: DFT testing was completed in n=11 pigs (39.3 ± 9.5 kg). See graph for results. Average shock impedances were 38.9 ± 3.3 Ω (TV), 37.7 ± 5.4 Ω (SS) and 43.2 ± 8.8 Ω (SQ).
Conclusions: The novel substernal-lateral configuration produced DFTs that were markedly lower than SQ DFTs and closer in value to TV DFTs. For humans, where the average TV DFT is ~10 Joules (J), the mean SS DFT would be ~15 J. Substernal therapy delivery may represent a clinically meaningful solution for treating cardiac arrhythmia, overcoming the high energy requirements and increased device size of SQ ICDs.

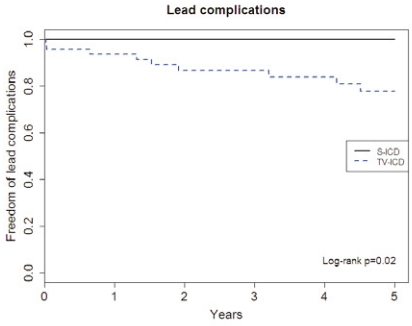


AB26-04

COMPARISON OF COMPLICATIONS AND SHOCKS IN PEDIATRIC AND YOUNG SUBCUTANENOUS AND TRANSVENOUS IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR PATIENTS

Anne-Floor BE. Quast, MD, Tom F. Brouwer, MD, Kirsten M. Kooiman, PA, Pascal FHM. Van Dessel, PhD, Arthur AM. Wilde, PhD and Reinoud E. Knops, MD. Academic Medical Centre, Amsterdam, Netherlands, Medisch Spectrum Twente, Enschede, Netherlands

Introduction: Young implantable cardioverter-defibrillator (ICD) patients are prone for complications and inappropriate shocks (IAS). The subcutaneous ICD (S-ICD) may avoid lead related complications. To our knowledge this is the largest cohort to date comparing complications and shocks of S-ICD and transvenous ICD (TV-ICD) in children and young adults.
Methods: All consecutive de novo single chamber TV-ICD and S-ICD patients <26 years implanted in our center between 2002 and 2015 were retrospectively analyzed. Device complications were defined as complications requiring surgical intervention and IAS as shocks not for VT/VF. Kaplan Meier estimates for complications at 5 year follow-up were calculated with corresponding 95%CI.
Results: A total of 46 TV-ICD patients (median at implant age 17 years) and 35 S-ICD patients (median age at implant 19 years) were included, median follow-up is 78 and 25 months respectively. All cause complications did not differ significantly, 34% in the TV-ICD arm and 25% in the S-ICD arm (p= 0.64). However TV-ICD patients had more lead complications 23% (9%-35%) versus 0% (p=0.02) (figure) and S-ICD patients had more infections 10% (1%-25%) versus 2% (0%-6%) (p=0.14). All infections were local. Appropriate shocks were similar, TV-ICD 22% (8%-36%) versus S-ICD 25% (4%-46%) (p=0.85), as was IAS rate 19% (7%-31%) versus 17% (1%-33%) (p=0.50).
Conclusions: All cause complications in this cohort were equal, however TV-ICD patients suffered more lead complications. Appropriate and inappropriate therapy was similar. Our data confirms the expected reduction of lead complications with use of the S-ICD in this high risk population.



AB26-05

WORLDWIDE CLINICAL EXPERIENCE OF THE RETRIEVAL OF LEADLESS CARDIAC PACEMAKERS

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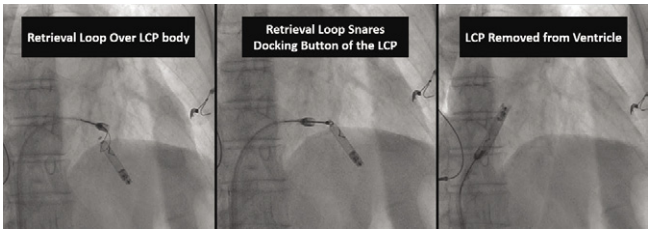
Introduction: Leadless cardiac pacemakers (LCPs) address certain device and lead related complications of transvenous pacemakers, but patients occasionally require device system upgrade, or require new devices for battery depletion. Retrievability is a desirable feature of implanted LCPs. We report the retrieval experience of the Nanostim LCP post-implantation in worldwide clinical studies.
Methods: Patients receiving a right ventricular active-fixation LCP (Nanostim, St. Jude Medical, USA) within two multicenter clinical trials conducted in Europe, US, Canada and Australia, and required device retrieval were included in this analysis. The presence of any serious adverse device effects (SADEs) up to 30 days after retrieval was documented.
Results: As of Nov 30, 2015, a total of 1006 patients were enrolled within two multicenter trials. Twelve patients (78.9 ± 12 yrs, 75% male) implanted with the LCP underwent retrieval attempts (9 centers, 9 operators). The reasons for retrieval were: elevated pacing thresholds (6 pts), worsening heart failure (5 pts), and elective explantation (1 pt). Five patients received new LCPs, 2 received conventional dual-chamber pacemakers, and 5 heart failure patients received CRT devices. The timing of LCP retrieval was 197 ± 190 days (median = 154 days; range = 1 to 506 days) with a Nanostim retrieval catheter without any SADEs (including no pericardial tamponade); four patients had received the LCP implant over 1 year prior to retrieval.
Conclusions: The Nanostim LCP proved to be safely and successfully retrievable in patients up to ~1.5 years post-implantation.



ABSTRACT AB27:
New CIED Implantation Concepts

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB27-01

LONGTERM OUTCOMES IN LEADLESS MICRA TRANSCATHETER PACEMAKERS WITH ELEVATED THRESHOLDS AT IMPLANTATION

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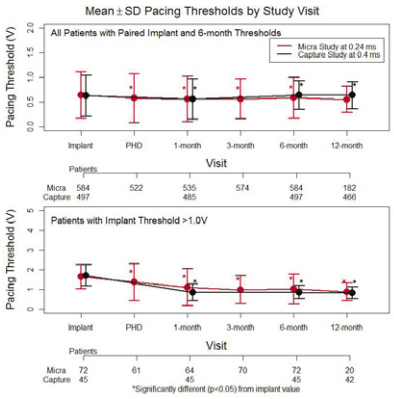
Introduction: The Micra transcatheter pacemaker is safe and effective; however, device repositioning may be required for optimal thresholds. Multiple repositioning is associated with a small but increased risk of adverse events at implant. While thresholds may be elevated after initial deployment, the natural history of elevated high capture thresholds in the Micra device is not well-defined.
Methods: Micra study VVI patients (pts) with threshold data (at 0.24 msec) at implant (n=711) were compared with Capture study pts with de novo transvenous leads at 0.4 msec (n=538). In both cohorts, high pacing thresholds were defined as >1.0V and very high as >1.5V. Change in pacing threshold (0 to 6 months) with high (1.0 - <1.5V) or very high (>1.5V) thresholds were compared using the Wilcoxon signed rank test.
Results: Among 711 Micra pts, 83 (11.7%) pts had an implant threshold >1.0V at 0.24 ms. Among 538 Capture pts, 50 (9.3%) had an implant threshold of >1.0V at 0.40 ms. There were no significant differences in pt characteristics or electrode location between pts with and without an implant threshold >1.0V, with the exception of LVEF in the Capture cohort (lower with high thresholds, 53 vs 58%, p=0.011). On average pts had low thresholds and pts with implant thresholds >1.0V decreased significantly (p<0.001) in both cohorts (Figure). Micra pts with high and very high thresholds decreased significantly (p<0.01) by 1-month with 87% and 85% having 6-month thresholds lower than the implant value.
Conclusions: Capture threshold in most Micra pts with elevated thresholds decrease after implant. These data suggest that Micra device repositioning may not be necessary if the capture threshold is <1 to 1.5V.



AB27-02

FEASIBILITY OF EXTRAVASCULAR PACING WITH A NOVEL SUBSTERNAL ELECTRODE CONFIGURATION: RESULTS FROM THE MULTI-CENTER SUBSTERNAL PACING ACUTE CLINICAL EVALUATION (SPACE) TRIAL

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Introduction: Subcutaneous defibrillators offer a viable alternative to intravascular transvenous defibrillators. However, because of extra-thoracic lead placement, this system is limited by high defibrillation thresholds and an inability to deliver anti-tachycardia pacing. The SPACE trial evaluated the feasibility of cardiac pacing from an extra-vascular substernal space.
Methods: This prospective feasibility study enrolled adult patients (pts) undergoing midline sternotomy surgery or S-ICD implant. The primary endpoint was to assess the feasibility of pacing through a decapolar EP catheter (Marinr, 7F, Medtronic) temporarily placed via percutaneous subxiphoid access into the mediastinal tissues under the sternum at or adjacent to the midline. Using fluoroscopy and a malleable tunneling tool and introducer, the middle pair of electrodes was centered over the right ventricle. Pacing capture data in 7 vectors (3 bipolar and 4 unipolar) were collected with constant current pacing up to 20 mA and pulse-width (PW) up to 10 ms.
Results: Twenty-four pts (19 males, 5 females; age 64.1 ± 10.3 years) were studied at 8 sites in the US and Canada. Parent procedures included one S-ICD implantation and 23 cardiothoracic surgeries. Catheter placement was accomplished

in all 24 pts (mean placement time = 13.4 ± 11.0 minutes). Seventeen out of 24 pts had successful, consistent ventricular pacing capture (PC) in ≥ 1 tested vector. The mean pacing thresholds at PW 10 ms, 3 ms, 1 ms were 7.0 ± 4.4 mA (17 pts), 9.0 ± 4.7 mA (13 pts), 11.8 ± 4.5 mA (7 pts), respectively. Failed PC in 7 pts was mostly associated with sub-optimal implant or atrial PC. Among the 17 pts with PC, 11 pts had the best PC in bipolar vs 5 pts in unipolar (no difference in 1 pt). Among the 15 pts with bipolar PC, widely spaced bipolar electrode pairs were consistently associated with the lowest threshold in all pts. For the 15 pts with bipolar PC with electrode spacing 19 mm and 10 ms PW, the median pacing threshold was 2.9 V (IQR: 2.2-8.0 V) or 4.1 mA (IQR: 3.0-10.0 mA).
Conclusions: Preliminary data demonstrates that pacing is feasible from this novel extravascular substernal location. A bipolar substernal electrode configuration with wide electrode spacing has the potential to provide pacing in a future extravascular defibrillator.

AB27-03

EFFICACY AND PERFORMANCE OF TRANSVENOUS AND EPICARDIAL LEFT VENTRICULAR LEADS IN A FIVE YEAR FOLLOW UP PERIOD

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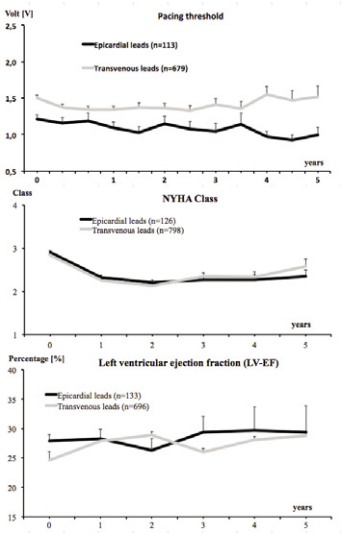
Introduction: Cardiac resynchronization therapy (CRT) is the gold standard in severe heart failure therapy if medical treatment fails. Well-functioning transvenous (tLV) or epicardial (eLV) left ventricular leads are essential for sufficient CRT therapy. However, only few studies compare long-term follow-up of both lead types.
Methods: We retrospectively analyzed left ventricular lead function (834 tLV/146 eLV) and ventricular remodeling in 980 consecutive CRT patients. Patient characteristics, sensing, pacing threshold, impedance, NYHA class, ejection fraction (LV-EF), end-systolic (LVESD) and end-diastolic LV-diameter (LVEDD) were assessed annually with 5-year follow-up.
Results: There were no differences in baseline characteristics between both groups. Pacing threshold remained robust, tLV sensing decreased (13.5mV to 12.5mV) and eLV increased (11.6mV to 17.3mV) over time. In tLV leads, impedances showed a moderate decrease, in eLV impedances returned to basic values after an initial drop (596Ohm to 512Ohm). LV-EF increased in tLV (24.6% to 28.8%) and eLV group (27.9% to 29.4%). Preoperative LVESD was 57mm (tLV) and 54mm (eLV) and did not change after an initial decrease. LVEDD remained almost unchanged in both groups (tLV 66mm and eLV 64mm). NYHA class improved significantly (tLV 2.8 to 2.6 and eLV 2.9 to 2.4).
Conclusions: Both lead concepts showed excellent long-term performance. Echocardiographic parameters confirmed effective CRT therapy after implantation. No significant differences between tLV and eLV could be detected. Transvenous and epicardial leads are equivalent alternatives for LV pacing.



AB27-04

FIRST IN VIVO RESULTS OF A 'TRULY' MINIMALLY INVASIVE EPICARDIAL PACEMAKER LEAD IMPLANTATION METHOD

Bjoern Peters, MD, Florian Gross, No Degree, Boris Schmitt, MD, Marco Bartosch, No Degree, Heiner Peters, No Degree and Felix Berger, PhD. German Heart Institute Berlin, Berlin, Germany

Introduction: Epicardial leads are currently the only therapeutic alternative when the standard transvenous approach is not applicable. Epicardial pacing allows more physiological left ventricular stimulation and avoids common vascular problems. In order to minimize trauma associated with open heart surgery a fast, easy and reliable minimally invasive epicardial lead implantation method was developed. A 3D steerable catheter was designed to deliver prototype bipolar screw-in leads to atrial and ventricular target sites.
Methods: In 14 pigs (14.7±1.8 kg) pericardial access was established via subxiphoidal micro puncture to introduce steerable delivery catheters under fluoroscopy guidance. Leads were fixed in atrial and ventricular position and correct function confirmed by measurement of intrinsic P/R wave signal, pacing threshold (PT) and lead impedance. Before and after lead placement cardiac structures and coronary arteries were visualized by angiography.
Results: We successfully implanted and evaluated atrial and ventricular leads in all 14 animals. No major procedural complications occurred, one animal died of ventricular fibrillation caused by severe hypokalemia after the procedure. Absence of vascular injury was documented by coronary angiography for all animals and procedural safety proven. For atrial leads P wave was 3.8±3.6 mV and PT 0.7±0.3 V @0.5ms. Impedance ranged from 417-1443 Ohm (mean 720). For the ventricular leads R signal was 11.6±7.5 (3.0-29.3) and PT 0.7±0.4 (0.3-1.5) V @0.5ms; impedance ranged from 452-1318 Ohm (mean 805). Dual chamber pacing was possible in all animals.
Conclusions: The presented data demonstrates the general feasibility of this minimally invasive method with good acute lead performance. The approach combines the advantage of true selective site pacing with the simplicity of the transvenous lead delivery. Long term follow up trials are currently performed to establish this method as a clinical alternative.

AB27-05

USE OF SURGICAL HEMOSTATIC POWDER FOR EP DEVICE IMPLANTATION REDUCES POSTOPERATIVE RATES OF POCKET HEMATOMA AND INFECTION

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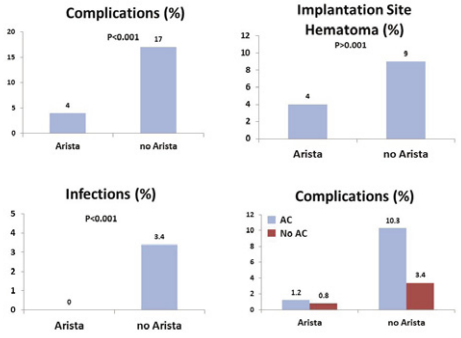
Introduction: Surgical site bleeding and infection could be potential complications after EP device implantation procedures. The success of a procedure can often depend on a surgeon's ability to efficiently and effectively control bleeding particularly when anticoagulation (AC) is on board. To date there is a wide variety of tools for management of intraoperative bleeding but it still remains unclear what methods are preferred.
Methods: In our study, a new plant-derived microporous polysaccharide hemostatic powder (ARISTA) was used. Our retrospective study included 283 consecutive patients (2013-2014) who underwent EP device implantation with the use of Arista (n=77, Arista) and without (n=206, No-Arista). We assessed the rate of complications in both patient groups. All patients were followed for 12 wks.
Results: Arista group patients had lower complications rate when compared to No-Arista: 4% versus 17 % (p<0.001), respectively. Rate of device implantation site hematoma in Arista group was 4%, vs 9% in the other group, (p>0.001). There were no postoperative infections in the Arista group versus 7(3.4%) infections in the No-Arista group. Among the all patients 13% were on systemic AC, 4.5% in the Arista group and 8.5% in no-Arista group. One of the predictors of increased risk of post-procedural complications was systemic AC with HR 2.7, while using Arista was associated with 3 times reduced risk of complications.
Conclusions: Using Arista for the post-procedural hemostasis was shown to be safe and resulted in significant reduction of the rate of post-procedural complications, as well as rate of infections. The trend of reduction in the rate of device implantation site hematoma was noted.



AB27-06

DRAMATIC RISE IN CARDIAC IMPLANTABLE ELECTRICAL DEVICES; WHO IS AT GREATER RISK?

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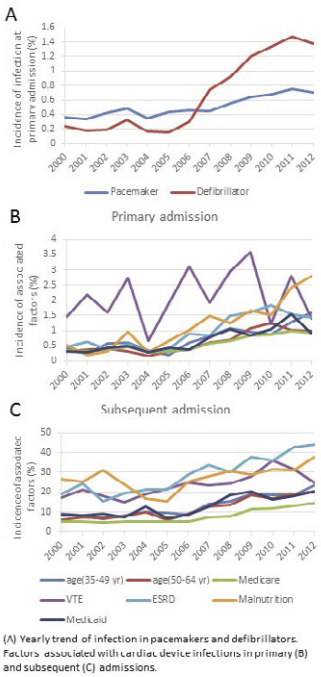
Introduction: We have noted an increase in infections of Cardiac Implantable Electrical Devices (CIEDs). Our purpose was to determine the difference in rates of infections between the ICDs and pacemakers and associated conditions that may affect that risk.
Methods: Nationwide Inpatient Sample 2000 to 2012 database was utilized. ICD-9-CM procedure codes for CIED-related procedures were combined with device-related infection code (996.61) or evidence of infection like sepsis (038 or 785.59), bacteremia (790.7), or fever (780.6) to estimate infection burden. Clinically relevant comorbidities associated with device infections were found by multiple regression and yearly trend was analyzed.
Results: There were 3,648,015 primary admissions for device-related procedures in patients without a history of CIED infections. Of these 1,212,118 were ICD-related procedures of which 0.66% were secondary to infection; 2,435,897 were pacemaker procedures with 0.50% secondary to infection (p=0.00). From 2005 to 2012, 762% rise in ICD infections were encountered at primary admission, that is greater than 95% rise in pacemakers (Panel A). Factors that showed a rising association with CIED infections are the following:35-64 year age group (vs 18-34 years), Medicare & Medicaid (vs private insurance), venous thromboembolism, end-stage renal disease (ESRD) and malnutrition (Panel B & C).
Conclusions: Risk of CIED infections is increasing but at a greater rate in patients receiving an ICD rather than a pacemaker. While ESRD and malnutrition are associated with recurrent CIED-related infections, the cause for the greater increased risk in those receiving ICD and the rise over time remains inconclusive.



(A) Yearly trend of infection in pacemakers and defibrillators. Factors associated with cardiac device infections in primary (B) and subsequent (C) admissions.

ABSTRACT PLUS AB28: New Concepts in Lead Extraction

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB28-01

UTILITY OF INTRACARDIAC ECHOCARDIOGRAPHY DURING IMPLANTABLE CARDIAC DEVICE PERCUTANEOUS EXTRACTION: A SINGLE CENTER EXPERIENCE FROM A TERTIARY MEDICAL CENTER

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Introduction: As the number of patients receiving implantable cardiac devices has increased, so has the need for device extraction. Despite technical advances, extraction remains a challenging procedure with risk of major vascular complications. Intracardiac echocardiography (ICE) is a supportive and diagnostic tool in a variety of cardiac procedures. We describe our utilization of using ICE during lead extraction.
Methods: Single center extraction records were reviewed from 2009-2015 for patients who underwent device/lead extraction, where ICE was also used. We reviewed inpatient and outpatient records. ICE images were obtained using a phased array probe.
Results: ICE was used in 429 extraction procedures. 998 leads with an average age of 78 +/- 48 months were succesfully extracted. The average extraction time per lead was 15 +/- 20 minutes. Major complications occurred in 13 patients (cardiac tamponade source not specified (4), superior vena cava tear/perforation (2), right venticular perforation (2), atrial laceration (1), coronary sinus tear/perforation (2) flail tricuspid valve (1) and subclavian vein perforation (1)). Timely identification of complications with ICE allowed for rapid interventions (pericardiocentesis (5), sternotomy (5) and chest tube placement (3). Of patients sustaining a major vascular complication, the survival rate was 93.3%. ICE identified intracardiac vegetations in 153 patients, 33 vegetations were seen on the tricuspid valve, 119 on device leads, 4 on the RA-SVC junction and 3 on the aortic valve. 33 patients were found to have extraction casts post procedure that were not seen pre-procedureally. There were no complications associated with the ICE probe.
Conclusions: ICE imaging during device extraction is safe and allows for visualization of vegetations and provides rapid identification of complications leading to prompt intervention.

AB28-02

COMPARISON OF TRANS-ESOPHAGEAL ECHOCARDIOGRAPHY AND FDG PET/CT IN THE DIAGNOSIS OF IMPLANTED DEVICE LEAD ENDOCARDITIS

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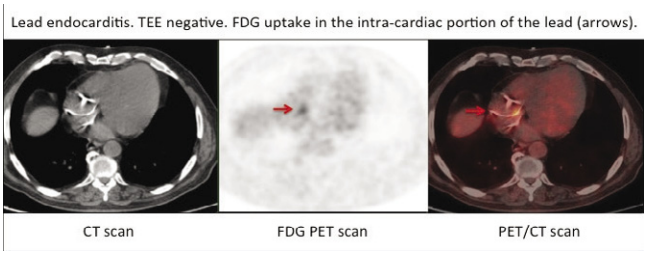
Introduction: 18-fluorodeoxyglucose positron emission tomography/computerized tomography (FDG PET/CT) scan has been proposed as a diagnostic tool for cardiac implantable electronic device (CIED) infection. We investigated the role of FDG PET/CT for the diagnosis of lead endocarditis as compared to conventional trans-esophageal echocardiography (TEE).
Methods: Patients with a confirmed diagnosis of lead endocarditis (positive lead culture after extraction of the suspected CIED) were included in the study. A TEE and a FDG PET/CT scan were performed before extraction and each analyzed blindly to assess for the presence of a lead infection (vegetation and FDG uptake along the device leads).
Results: 41 consecutive pts (73 ±13 years, 36 male) were studied. At the time of imaging 59% of pts were on antibiotics. TEE identified a lead vegetation in 12 pts (29%); they ranged 2 to 20 mm in size. On FDG PET/CT there was increased uptake along the lead in 33 pts (80%), and along the intra-cardiac portion of the device in 22 pts (54%). Of the 22 patients with a positive intra-cardiac portion on PET/CT, 16 (73%) did not demonstrate a vegetation on TEE. On PET/CT there was increased uptake along the extra-cardiac portion of the lead in 30 pts (73%). When used together, TEE or PET/CT scan identified 38 pts (93%) with lead endocarditis. With PET/CT septic emboli were identified in 9 pts (22%): 4 with spondylodiscitis, 4 with septic pulmonary emboli and 1 with an infected vascular prosthesis.
Conclusions: Compared to PET/CT, TEE is less sensitive in detecting implanted lead endocarditis. When used synergistically with TEE it confers higher sensitivity of detecting lead infections, including extra-cardiac involvement.



AB28-03

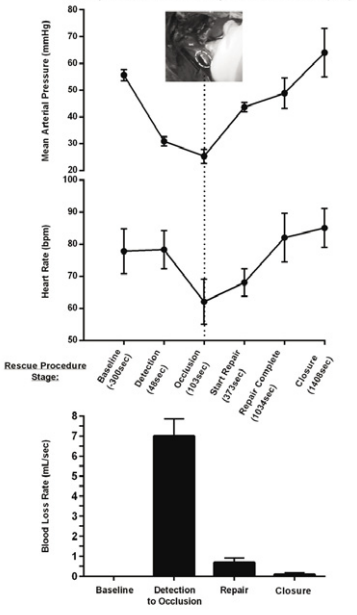
ENDOVASCULAR MANAGEMENT OF SVC INJURY WITH NOVEL OCCLUSION BALLOON IN A PORCINE MODEL

Jude Clancy, MD, Roger G. Carrillo, MD, Ryan Sotak, BS, Rashmi Ram, PhD and Charles Kennergren, MD. Yale University School of Medicine, New Haven, CT, University of Miami Hospital, Miami, FL, Spectranetics Corporation, Colorado Springs, CO, Sahlgrenska University Hospital, Gothenburg, Sweden

Introduction: While extremely rare, superior vena cava (SVC) injury can be life threatening if not treated instantly. Preventing major hypovolemia following injury can improve patient outcomes. We evaluated an SVC tear rescue procedure using a novel occlusion balloon in a porcine model.
Methods: Seven (n=7) pigs had 2 transvenous pacing leads placed into the RV. Following baseline hemodynamics, a sternotomy was created and the pericardium opened. After side-clamping the SVC, a 2cm surgical tear was created on the lateral wall. The clamp was released creating major bleeding into the right pleural space. An occlusion balloon (Bridge™ Occlusion Balloon; Spectranetics) was quickly advanced to the tear location through femoral vein access and inflated. Following hemodynamic stabilization, surgical repair of the tear was performed by clamping and direct suturing or by SVC reconstruction with pericardial patch. Animals were monitored for

5 days postoperative for behavioral and neurologic function.
Results: Mean arterial pressure recovered after hypovolemia with use of occlusion balloon and transfusion (Figure 1). The blood loss rate reduced on average from 7.0 to 0.7mL/sec following occlusion. Study animals displayed stable recovery and uneventful neurologic and behavioral outcomes to postoperative day 5.
Conclusions: Use of a novel occlusion balloon in the SVC successfully controlled bleeding during injury repair and was instrumental to animal survival. This novel device may provide a path to improved outcomes following SVC injury from lead extraction procedures.

Figure 1:
Hemodynamic Measures During Rescue Procedure (n=4)



AB28-04

PERCUTANEOUS VACUUM-ASSISTED THROMBECTOMY DEVICE USED FOR REMOVAL OF LARGE VEGETATIONS ON INFECTED PACEMAKER AND DEFIBRILLATOR LEADS AS AN ADJUNCT TO LEAD EXTRACTION

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Introduction: Early experience with a minimally invasive percutaneous method of safely removing large vegetations during lead extraction in septic cardiac rhythm management (CRM) devices. Debate exists concerning the management of vegetations involving CRM devices. Lead extraction is mandated for infections, but during extractions, vegetations may embolize, causing complications. Surgical debridement is often recommended. Options include cardiopulmonary bypass or minimally invasive thoracotomy. This describes our first twelve consecutive patients, all critically ill with sepsis despite long-term antibiotics, and vegetations.
Methods: The AngioVac was used to debulk and/or remove infective vegetations before percutaneous lead extraction in the same setting. The AngioVac system allows percutaneous right heart bypass and ability to suction vegetations under echocardiographic guidance. The distal tip of the large bore cannula has a balloon-actuated, expandable, funnel-shaped tip. An inline filter traps intravascular debris while returning blood to the patient and maintaining hemodynamic stability with a veno-venous extracorporeal bypass circuit.
Results: All twelve patients survived the procedure and resolved their infections. The mean patient age was 80 years. The average vegetation size was 3.7cm. Setup of the procedure averaged 10 minutes. One intraprocedural complication, an injury to an iliac vein, occurred and was repaired with a stent. The average length of stay was 3.6 days. Case 3 stayed an extra three days to have an unrelated procedure. Case 4 was a Jehovah's Witness; the patient had preoperative and postoperative hemoglobin levels of 9 and 3 mg/dL, contributing to the extended length of stay.
Conclusions: The AngioVac system is a safe and effective alternative to surgery in treatment of septic patients with large lead vegetations.

AB28-05

OUTCOMES OF TRANSVENOUS LEAD EXTRACTION FOR CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICE INFECTIONS IN PATIENTS WITH PROSTHETIC HEART VALVES

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Introduction: Lead-related or valve-related endocarditis can complicate cardiovascular implantable electronic device (CIED) infection in patients with both CIED and prosthetic valves. The objective of this study was to determine outcomes of transvenous lead extraction for CIED infection in patients with prosthetic valves.
Methods: We retrospectively screened 794 transvenous lead extraction procedures between September 1, 2001 and August 31, 2012 at Mayo Clinic to identify patients with prosthetic valves who underwent lead extraction for infection. Demographic, clinical, and follow-up characteristics were analyzed.
Results: In total, 51 patients (6%) met study inclusion criteria, of whom 20 had pocket infection (PI group) and 31 had lead-related or valve-related, or both, endocarditis or bloodstream infection (IE group) (mean age, 67 (18) years). Staphylococcal species were the most common pathogens, including Staphylococcus aureus in 20 cases (39%) and coagulase-negative staphylococci in 19 cases (37%). Overall, 127 transvenous leads (median lead age, 52 months) were extracted. Of these leads, 123 (97%) were removed completely. The in-hospital mortality rate was 9.8%; no deaths were attributable to the extraction procedure. Ninety-two percent of study patients had no evidence of recurrent device-related or valve-related infection.
Conclusions: Transvenous lead extraction appears safe and curative in patients with CIED infection and prosthetic valves. Cure of infection can be achieved in the majority of patients with complete CIED removal and antimicrobial therapy and without valve surgery.

ABSTRACT AB29:
New Ablation Technologies

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB29-01

IRON NANOPARTICLES ENCASED WITHIN HEAT SENSITIVE LIPOSOMES CAN BE MAGNETICALLY GUIDED AND WILL ENHANCE RADIOFREQUENCY ABLATION

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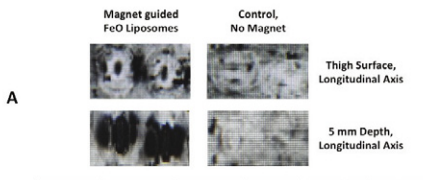
Introduction: Various facilitating agents, including gadolinium and iron oxide (FeO), can enhance radiofrequency ablation (RFA) of cardiac tissue. However, direct injection as a delivery method for these agents limit their use. We sought to evaluate the use of heat-sensitive liposomes as a systemic delivery system to provide precise and localized targeting of tissue with RFA.
Methods: FeO nanoparticles (NPs) were encased in heat-sensitive liposomes and systemically infused during RFA using an in vivo porcine thigh model. Magnets were used to guide the liposomal FeO NPs to RFA sites, where RF heating released FeO NPs from their liposomes. MRI was performed of ablated tissue to confirm the presence of FeO.
Results: Magnet-guided localization of liposomal FeO NPs within thigh preps was demonstrated by MRI (Figure). After liposomal FeO NP infusion and magnetic guidance, irrigated ablation in regions with greater FeO deposition generated larger lesions without a greater incidence of steam pops, compared to control tissues ablated after no liposomal infusion (Figure).
Conclusions: Heat sensitive liposomes can be used to encase facilitating agents such as FeO NPs, which can then be directed magnetically and released from their liposomes with RF heating. Once FeO NPs are locally discharged, they can amplify RFA at the target RF site by inductive heating. Heat-sensitive liposomes may limit systemic side effects, as their payloads will only be released locally. Further research is needed to evaluate the clinical applicability of this delivery system to enhance RFA for treating cardiac arrhythmias.



B

		Average Max Depth (mm)	Diameter Max (mm)	Max Surface Diam (mm)	Volume (mm^3)
Untreated	(n=20)	5.2±0.7	10.1±1.1	7.5±1.0	189.5±54.5
Liposomal iron	(n=23)	7.1±1.1	13.1±1.5	9.1±1.5	379.7±114.8
p-value	Liposomal iron vs. Untreated	p < 0.001	p < 0.001	p < 0.001	p < 0.001

(A) MRI of ablated porcine thigh preps after magnet-guided iron oxide (FeO) liposomal infusion to RF sites vs control (FeO liposomal infusion but no magnet guidance). **(B)** Table of lesion sizes for RFA of thigh preps after magnet guided liposomal FeO infusion vs controls (untreated).

AB29-02

FIRST-IN-MAN TREATMENT OF ATRIAL FIBRILLATION USING CARDIAC RADIOSURGERY

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Introduction: Cardiac stereotactic radiosurgery (CSR) for tachyarrhythmias represents a painless, minimally invasive ablative option for patients that have failed or are not candidates for therapy with drugs or conventional ablation. CSR has been applied previously to patients with refractory ventricular tachycardia that have failed or were not eligible for catheter ablation. Radiosurgery offers pinpoint ablation accuracy, even with cardiac and respiratory motion. A 58 year old patient with drug-refractory paroxysmal-persistent atrial fibrillation (AF) was offered cardiac stereotactic radiosurgery atrial ablation following a recovered stroke secondary to atrial fibrillation.
Methods: Following informed consent, a cardiac gated CT scan was obtained to delineate atrial anatomy. Following placement of a percutaneous right atrial fiducial, CT scan data was delivered to CardioPlan™ (the electrophysiology proprietary software to contour ablation volumes) and to the Multiplan™ software of a Cyberknife. The electrophysiologist contoured where he desired the ablation volumes to be located. In this particular case, a modified 'box' isolation lesion set was fashioned to create scar sufficient to electrically isolate all four pulmonary veins and the left atrial posterior wall. Contours from CardioPlan were transferred to Multiplan and treatment confirmed that a safe treatment plan could be accomplished. The treatment (25 Gy) took approximately 2. 5 hours, was performed in one fraction, without the need for any sedation. Atrial ablation volume was 2.1 cm3. Late gadolinium enhanced of a cardiovascular MRI demonstrated left atrial scar corresponding to placement of ablation targets. The fiducial was then removed.
Results: There were no treatment related adverse events. Anti-arrhythmic medications were discontinued at 6 months post treatment with confirmation of predominant sinus rhythm. NOAC therapy was continued. CT scans showed no evidence of pulmonary vein stenosis, pericardial effusion, of change in ejection fraction or mitral valve dysfunction post treatment.
Conclusions: Cardiac stereotactic radiosurgery was safely and effectively delivered to a patient with drug-refractory AF. Further study is warranted.

AB29-03

IMPACT OF MECHANICAL VIBRATION RF ABLATION COMPARED WITH CONVENTIONAL RF ABLATIONS

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Introduction: We have newly developed RF ablation catheter that can vibrate the tip of electrode with RF administration. The feasibility of this vibration ablation catheter was evaluated by comparing with ordinal 4mm tip and irrigation catheter.
Methods: The coagulation efficacy of 4mm tip vibration catheter (Vib) was compared with 4mm tip irrigation catheter (Irr) and 4mm tip non-irrigation catheter(Cont) using a cut swine heart muscle (30×20×15 mm)in the saline bath at temperature of 37 °C. For the vibration catheter, ablation was done with ±1mm horizontal vibration 63Hz and temperature control at 60°C. For the irrigation catheter, the condition was 30W power control with 17ml/ min irrigation. For the ordinal 4mm tip ablation was done with temperature control at 60°C. Ablation durations were 60 sec in both methods, and the lesion sizes were measured by maximum diameter and maximum depth of lesions stained by

TTC.
Results: The total energies applied in three conditions were 1750±150 Joule(Vib), 1600±220Joule (Vib) and 600±120 Joule (Cont). The maximal depth of lesions were 6.2±0.3mm(Vib), 5.5±0.4mm(Irr) and 2±0.2mm(Cont). The maximal diameter of lesions were 12.0±0.4mm(Vib), 8.5±0.02mm (Irr) and 5.1±0.05mm(Cont). Vib and Irr made more large lesions than Cont ($p<0.005$). There were no significant differences in lesion sizes between Vib and Irr.
Conclusions: Newly developed vibration RF catheter was comparable to irrigation catheter without water hydration for catheter ablation.

AB29-04

INDUCIBILITY OF ATRIAL FIBRILLATION AFTER EPICARDIAL INJECTION OF THE NEW PHARMACEUTICAL COMPOSITION CONTAINING BOTULINUM TOXIN INTO EPICARDIAL FAT PADS

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Introduction: Prior clinical and animal studies suggest that botulinum toxin injection into the epicardial fat pads can suppress AF recurrences and inducibility. However, currently known botulinum toxin compositions do not have a prolonged action, nor increase the therapeutic effect of botulinum toxin and are not intended to treat cardiac arrhythmias. The aim of the present study was to assess the efficacy and safety of the new pharmaceutical composition containing botulinum toxin and mucopolysaccharide injection into epicardial fat pads for prevention of AF.
Methods: 24 dogs were separated into 3 groups: epicardial approach for the new pharmaceutical composition containing botulinum toxin and mucopolysaccharide (chitosan; WO2014184746 A1) injection into 3 main epicardial fat pads, epicardial approach for placebo (normal saline) injection (control 1; n=8) and epicardial approach for pure botulinum toxin injection (control 2; n=8).
Results: 3 epicardial injections (50 unit of botulinum toxin per 1 mL at each) were administrated into 3 main left atrial autonomic nervous system projection of each animal. Injections of all forms botulinum toxin demonstrated dramatic prolongation of ERP in all PV-atrial junctions and vagal stimulation shortened ERP was less pronounced. Suppression of AF inducibility was observed at day 7 after all forms botulinum toxin group injections. The reduction of AF inducibility after pure botulinum toxin injection was: at 7 day-57% ($p<0.001$ vs placebo; $p<0.001$ vs baseline); at 14 day - 61% ($p<0.001$ vs placebo; $p<0.001$ vs baseline); at 1 month - 38% ($p<0.001$ vs placebo; $p<0.001$ vs baseline); at 3 month-23% ($p=0.003$; $p=0.06$ vs baseline). Composition containing botulinum toxin and mucopolysaccharide showed the lowest AF inducibility and prolonged effect: at 7 day-86% ($p<0.05$ vs pure form); at 14 day-75% ($p<0.05$ vs pure form); at 1 month-71% ($p<0.05$ vs pure form); at 3 month-65% ($p<0.05$ vs pure form). No cardiac suppressive effect or significant procedure-related complications occurred.
Conclusions: Composition containing botulinum toxin and mucopolysaccharide injection into epicardial fat pads was feasible and safe, increased and prolonged effect of complete abolition of cardiac vagal responses and significant AF suppression.

AB29-05

BIOPHYSICS OF TISSUE ABLATION IN CATHETER-FREE ABLATION WITH CARBON ION BEAMS

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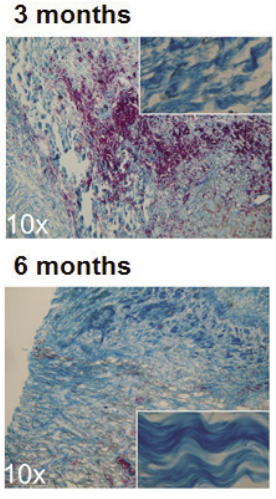
Introduction: Carbon ion (12C) beams can precisely deliver high doses of ionizing radiation to small targets through the body surface. We have recently provided feasibility data on cardiac tissue ablation using 12C in animal models. Here, we present the biophysical mechanism and time course of this form of tissue ablation.
Methods: Seventeen pigs were randomized to irradiation of AV junction (AVJ), right superior pulmonary vein LA junction (PVI), freewall LV, and sham. The AVJ was targeted with 25, 40, and 55 Gy. PVI and LV were targeted using 40 Gy. All ion beams were delivered using breath holds in end-expiration and a horizontal beam line. Animals were followed for three to six months after irradiation. Gross pathology, histological analysis using hematoxylin eosin and Mallory's Trichrome staining, protein extraction, and Western Blotting with analysis of apoptotic markers was conducted.
Results: Three months after irradiation, target doses of ≥40 Gy led to complete interruption of cardiac conduction. At that time, lesions were marked by a higher degree of hemorrhage and inflammation than lesions six months after irradiation (Figure). Doses of 25 Gy only led to minor fibrotic changes, while 40 and 55 Gy led to a strong fibrotic response. The apoptosis marker cleaved caspase 3 was present in irradiated tissue at three months of follow-up, but lesions were negative for cleaved caspase 3 six months after irradiation.
Conclusions: Ablation lesions induced by 12C are characterized by an inflammatory state and tissue apoptosis around three months after irradiation. Further lesion maturation leads to a decrease in inflammation with no ongoing apoptosis six months post-irradiation.



AB29-06

ALL-OPTICAL THROUGH-NEEDLE ULTRASOUND: A NEW IMAGING PARADIGM

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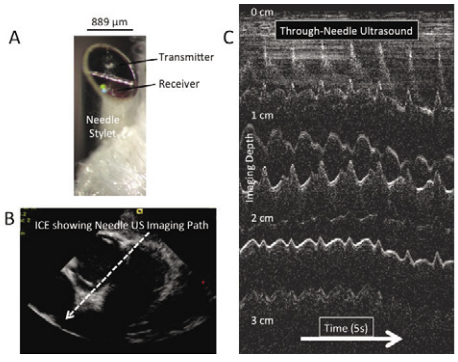
Introduction: Transseptal puncture (TSP) exemplifies the challenge of accurate guidance during interventional procedures. Ultrasound provides soft tissue visualization, but miniature electronic transducers are limited by cost & manufacturing complexity. We present a new paradigm for real-time guidance of interventional procedures called all-optical ultrasound, demonstrated by in vivo imaging of the forward path of an TSP needle stylet.
Methods: Imaging was performed with telecommunication-grade fiber optics positioned unobtrusively within an Endry's inner needle (internal diameter 889μm, Fig. A). Transmission was via the photoacoustic effect: modulated light, when delivered to an optically absorbing coating on the distal fiber tip, results in thermal deposition and hence ultrasound generation. Reception was via a Fabry-Pérot cavity on a second fiber, deformations caused by impinging sonic waves were detected as changes in optical reflectance. Studies were performed in swine under terminal anaesthesia, and monitored by intracardiac echocardiography (B) & fluoroscopy.
Results: Unprecedented views of in vivo cardiac structures were obtained directly ahead of the needle tip, image depths greater than 3cms with axial resolution finer than 70µm were achieved. Critical structures were readily identified, including valves, septum and far atrial wall (C). Distances to forward structures were evident with exquisite sensitivity during successful TSP.
Conclusions: All-optical ultrasound enables high-sensitivity imaging to be integrated into interventional devices. TSP and electrophysiology are the pioneer applications for this novel platform technology.



ABSTRACT AB30:
Determinants of Recurrence After AF Ablation

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB30-01

DETERMINANTS OF ACUTE AND LATE PULMONARY VEIN RECONNECTION IN CONTACT FORCE-GUIDED PULMONARY VEIN ISOLATION

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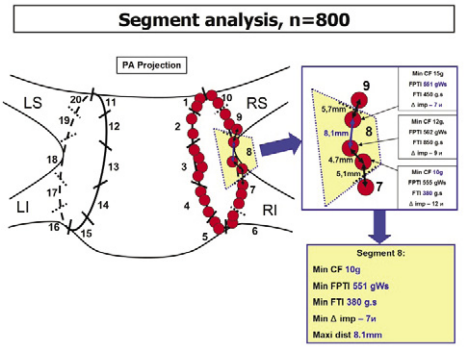
Introduction: After contact force (CF) guided pulmonary vein (PV) isolation, AF recurrence due to PV reconnection (PVR) occurs in up to 20 % of patients. We studied whether minimal CF (CFmin), minimal Force-Time-Integral (FTImin), minimal Force-Power-Time-Integral (FPTImin), minimal impedance drop (D-Impmin) and maximal interlesion distance (ILDmax) determine acute and late PVR.
Methods: Eligible patients (n=42) with symptomatic paroxysmal atrial fibrillation (AF) underwent ipsilateral PV isolation guided by CF sensing catheter (SmartTouch®, BSW) targeting minimal CF of 10g. PVI was obtained in 84 out of 84 circles (100%). Each ipsilateral circle was divided in 10 segments (5 posterior, 5 anterior). Acute PVR was defined as reconnection elicited by adenosine, late PVR as reconnection observed at repeat ablation in case of AF recurrence. For each segment CFmin, FTImin, FPTImin,D-Impmin and ILDmax.were analysed.
Results: 800 segments were analyzed. Acute PVR was observed in 25 segments (14 circles, 11 patients), late PVR in 19 segments (11 circles, 6 patients, median 6 months after first ablation). Compared to segments without PVR (n=758 segments), segments with PVR had lower CFmin (9 vs 12g, p $<$0.001), FTImin (367 vs 409 gs., p $<$0.007), FPTImin (351 vs 473 gWs., p=0.012), D-Impmin (5 vs 7Ω, p=0.049) and higher ILDmax (6.8 vs 6.0mm, p $<$0.001). There was no difference between anterior and posterior segments.
Conclusions: Parameters assessing lack of transmurality (CF, FTI, FPTI) and contiguity (ILD) are associated with acute and late PV reconnection after CF-guided PV isolation. These findings emphasize the need for a novel approach combining transmurality and contiguity.



AB30-02

MECHANISMS OF RECURRENCE AND LONG-TERM OUTCOMES IN PATIENTS WITH NON-PAROXYSMAL ATRIAL FIBRILLATION UNDERGOING LIMITED ABLATION WITH A STRATEGY COMPRISING PULMONARY VEIN ANTRAL ISOLATION AND NON-PULMONARY VEIN TRIGGER ABLATION

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Introduction: The optimal ablation strategy in patients (pts) with persistent (PS) and longstanding persistent (LP) atrial fibrillation (AF) is controversial. We aimed to determine mechanisms of recurrence and long-term outcomes in pts with PS and LP AF treated with pulmonary vein antral isolation (PVAI) and non-PV trigger ablation.
Methods: We identified consecutive pts with PS (n=200) and LP (n=200) AF undergoing first ablation and compared electrophysiologic characteristics and mechanisms of recurrence at each subsequent ablation. Pts had mobile continuous outpatient telemetry for 30d after ablation, and also at 6m and 12m. AF recurrence was defined as any AF or organized atrial tachycardia (AT) lasting >30s (excluding post-ablation blanking period).
Results: Of 400 pts (82% male; mean age 60.3y, duration since AF diagnosis 6.1y, LVEF 54±11%, LA diameter 4.7±0.7cm), AF/AT recurred in 228 (57%) over mean follow-up of 3.1±2.2y. Over this period, 100 pts had ≥1 redo ablation (19 with ≥2, 4 with ≥3, and 2 with 4 redos). PV reconnection and non-PV triggers were frequently seen. The number of reconnected PVs decreased (p<0.001) while the presence of non-PV triggers increased (p=0.045) in the third and subsequent ablations (Table). Overall 1y arrhythmia-free survival rate after last ablation in the entire 400 pt cohort was 70.3%.
Conclusions: In pts with PS and LS AF undergoing repeat ablation, PV reconnection is nearly universal at the first redo ablation; non-PV triggers are commonly seen on subsequent redo ablations. Achieving durable PVAI and ablating non-PV triggers at initial ablation are crucial to maximize long-term ablation success.

	2nd AF Ablation (n=100)	3rd AF ablation (n=19)	4th AF ablation (n=4)	5th AF ablation (n=2)	P value*
Long-standing persistent AF	56%	74%	75%	50%	0.494
Time since last PVAI (y)	1.8±1.6	1.7±1.8	2.2±1.6	0.9±0.8	0.819
Time since initial PVAI (y)	1.8±1.6	2.7±2.2	3.2±1.6	3.4±2.0	0.078
Electrophysiologic characteristics at time of repeat ablation					
PV reconnection indentified	93 (97%)	12 (71%)	4 (100%)	1 (50%)	0.009
Mean # of PVs reconnected	2.97 ± 1.2	1.7 ± 1.5	1.8 ± 0.5	1.0 ± 0.0	<0.001
Non-PV trigger identified	21 (22%)	8 (47%)	2 (50%)	1 (50%)	0.045
Long-term outcomes after repeat ablation					
Any recurrence after PVAI (excluding blanking period)	54 (55%)	9 (50%)	3 (75%)	1 (50%)	0.866
Mean time to recurrence after PVAI (d)	352 ± 342	183 ± 203	51 ± 16	668	0.155
Recurrence type after PVAI					0.115
• AF recurrence only	36 (37%)	5 (28%)	0 (0%)	1 (100%)	
• OAT recurrence only	8 (8%)	3 (17%)	3 (100%)	0 (0%)	
• Both AF and OAT recurrences	10 (10%)	1 (6%)	0 (0%)	0 (0%)	
Paroxysmal recurrence type only	19 (19%)	1 (6%)	0 (0%)	1 (50%)	0.382
1y freedom from arrhythmia recurrence	11 (61%)	11 (61%)	1 (25%)	2 (100%)	0.468

**P-value comparisons for second and subsequent ablations*

AB30-03

SURGICAL VERSUS PERCUTANEOUS AF ABLATION; A RANDOMIZED CONTROLLED TRIAL

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Introduction: The cornerstone of invasive AF treatment is pulmonary vein isolation (PVI). Both minimally invasive thoracoscopic epicardial PVI (MIPI) and percutaneously performed endocardial PVI are accepted treatments. As no randomized data is present for patients undergoing a first ablation, it is yet unclear which approach is most effective.
Methods: We conducted a randomized controlled trial in patients with lone, paroxysmal or persistent AF, undergoing a first ablation. Patients were randomized to MIPI with LAA excision or percutaneous PVI (PVI). RF energy was used for all ablations. All patients were monitored with implanted continuous loop monitors from 6 months before up to 2 years after the procedure. The primary outcome measure was freedom of atrial tachyarrhythmia. Results were analyzed on an intention to treat basis. The safety endpoint was freedom of complications, and was analyzed on an as treated basis.
Results: Between 2007 and 2013, fifty patients with drug-refractory AF were randomized to CA (n=25) or MIPI (n=25). Median age was 57 years (range 37-75), 78% were male and 74% had paroxysmal AF. All patients had 2 years of follow-up. No significant differences were present for the primary endpoint after 6 and 12 months follow-up. After 2 years, more patients were free of atrial tachyarrhythmia after PVI versus MIPI (12/25, 48% versus 5/24 21%, P=0.046). Although more procedure related complications occurred in the MIPI group, this did not reach statistical significance (3/25, 11% versus 6/24 26.1%, P=0.27).
Conclusions: Percutaneous PVI results in lower long-term AF recurrence rates than surgical PVI with LAA resection.

AB30-04

VERY LATE RECURRENCE OF ATRIAL FIBRILLATION 2 YEARS AFTER CATHETER ABLATION IS ASSOCIATED WITH METABOLIC FACTORS

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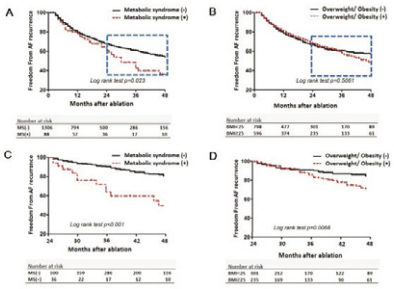
Introduction: Whether very late clinical recurrence of atrial fibrillation (AF) 2 years after radiofrequency catheter ablation (VLCR2-years) is related to AF progression remains unclear. We hypothesized that metabolic factors are associated with VLCL2-years.
Methods: Among 1394 patients who underwent catheter ablation, the study included 433 patients with AF recurrence (26.3% women, mean age 57±10 years, 57.6% paroxysmal AF) 3 months after the ablation procedure. They were further divided into the clinical recurrence (CR: AF recurrence at 3-24 months) and VLCR2-years (AF recurrence >24 months) groups.
Results: Over 38±17 months of follow-up, 346 (79.9%) and 87 (20.0%) patients formed the CR and VLCR2-years groups, respectively. The VLCR2-years group had higher proportions of obesity (BMI≥25Kg/m2, 58.6% vs. 41.6%, p=0.009), hypertension (74.6% vs. 63.5%, p<0.001), diabetes mellitus (25.3% vs. 18.7%, p=0.009), dyslipidemia (60.9% vs. 45.6%, p=0.010), high C-reactive protein (9.2% vs. 3.8%, p=0.035) and

metabolic syndrome score (2.17±0.98 vs. 1.80±1.07, p=0.007) than the CR group. In the multivariate analysis, obesity (odds ratio [OR] 1.819, 95% confidence interval [CI] 1.119-2.955, p=0.016), dyslipidemia (OR 1.677, 95% CI 1.028-2.737, p=0.038), and metabolic syndrome score (OR 1.466, 95% CI 1.136-1.891, p=0.003) were independently associated with VLCR2-years.
Conclusions: Obesity, dyslipidemia, and metabolic syndrome score are independent predictors of VLCR2-years for AF after catheter ablation. VLCR2-years seems to be affected by metabolic factors and can be related to AF progression.



AB30-05

IMPACT OF WEIGHT LOSS ON ABLATION-OUTCOME IN OBESE PATIENTS WITH LONG-STANDING PERSISTENT ATRIAL FIBRILLATION

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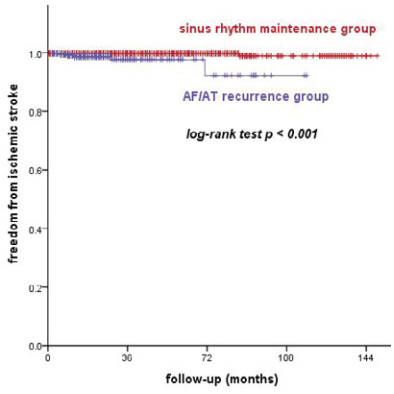
Introduction: Aggressive weight management reportedly causes significant decrease in arrhythmia burden and symptom severity, and improves ablation outcome in paroxysmal and persistent AF patients. This study investigated the impact of weight-loss on procedure outcome in long-standing persistent (LSPAF) patients undergoing catheter ablation (CA).
Methods: Ninety consecutive LSPAF patients with body weight >215 lbs [age 63±9 years, 72% male, weight 259 (IQR 216 -345) lb.] were approached; 58 volunteered to try weight-loss interventions with aggressive diet and exercise measures for up to 1 year (Group 1) while 32 patients declined for weight-loss interventions and included as control (Group 2).Both groups remained on anti-arrhythmic drugs (AAD). If they continued to experience AF, CA was offered to them. Body weight was measured at 6-months interval and arrhythmia status was assessed by event recorder, ECG and Holter monitoring. Symptom severity and QoL were evaluated by AFSS and SF-36 survey respectively. A scoring algorithm with two summary measures, PCS and MCS was prepared for QoL analysis.
Results: Baseline characteristics were similar between the two groups. After 1-year of the trial, significant reduction in body weight (median -55 (IQR -42 to -125) lb., p<0.001) was observed in the group 1 patients while no such change was seen in group 2. The PCS and MCS scores demonstrated substantial improvement in group 1 only, with a change from baseline of 8.4±3 (p=0.013) and 12.8±8.2 (p <0.02). However, AF symptom severity as measured by AFSS survey remained unchanged from baseline in both groups (p=0.84). All 90 patients underwent CA and received PVAI+ posterior wall+ non-PV triggers ablation. At 1-year follow-up after single procedure, 37 (63.8%) in group 1 and 19 (59.3%) patients in group 2 remained arrhythmia-free off-AAD (p=0.68).
Conclusions: In LSPAF patients, weight loss improved quality of life but had no impact on symptom severity and long-term ablation outcome.

AB30-06

STROKE RISK DURING LONG-TERM FOLLOW UP IN PATIENTS WITH SUCCESSFUL CATHETER ABLATION FOR ATRIAL FIBRILLATION

Dong-Hyeok Kim, MD, Young-Hoon Kim, PhD, Jong-Il Choi, PhD, Jaemin Shim, PhD, Dae In Lee, MD, Seung-Young Roh, MD, Jinhee Ahn, MD, Kwang No Lee, MD and Sang-Weon Park, PhD. Korea University Medical Center, Seoul, Republic of Korea

Introduction: Cessation of oral anticoagulation (OAC) after ablation of AF has been deemed controversial. In this study, we sought to evaluate the relation between long-term results of successful catheter ablation and the risk of ischemic stroke.
Methods: Total 1,548 consecutive patients who were eligible for follow up longer than 2 years after catheter ablation of AF were enrolled. The incidence of ischemic stroke during long-term follow up is investigated. .
Results: Compared to AF recurrence group (n=619), sinus rhythm (SR) maintenance group (n=929) had shorter time of AF onset (31 months vs. 46 months, p<0.001), more paroxysmal AF (75% vs. 44%, p<0.001), and less incidence of hypertension (29% vs. 35%, p=0.007). However, CHA2DS2-VASc score was not significantly different between two groups (0.9 vs. 1.1, p=0.053). The rate of ischemic stroke during mean 36 months of follow up after ablation was 0.6%, which was significantly lower in SR group than recurrence group (0.3% vs. 1.1%, log-rank test p<0.001, Figure). Sub-analysis in SR group, rate of OAC for patients with ≥4 CHA2DS2-VASc score is 16.7%. The rate of ischemic stroke was significantly higher in patients with ≥4 CHA2DS2-VASc score than those with less than 4 (4.3% vs. 0.2%, log-rank test p<0.001) in SR group.
Conclusions: This long-term follow up data in patients with AF who underwent catheter ablation showed that SR maintenance was related to lower rate of ischemic stroke, however, which was only observed in patients with CHA2DS2-VASc score ≤3.



ABSTRACT PLUS AB31: Novel Mapping and Ablation Technology: Improving Safety and Efficacy

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB31-01

CAVITARY POTENTIAL MAPPING: IMPLICATIONS TO SIGNAL PROCESSING IN MULTI-ELECTRODE ARRAY TECHNOLOGY

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Introduction: Bipolar electrograms (EGM) are traditionally measured by instrumentation amplifiers (hard wired) that require balanced impedance. As such improper contact will result in noisy signals. It is widely not recognized that current day electroanatomic mapping systems, CARTO, Velocity and Rhythmia use unipolar EGMs to derive bipolar EGMs. Given the fact that unipolar EGMs recordings are not sensitive to contact, it should be therefore possible to record derived bipolar EGM without contact to the myocardium. We hypothesized that using a collapsed ('non-contact') multielectrode array it is possible to record derived bipoles only if there exists cavitary potentials.
Methods: Five patients with diseased atria either due to congenital heart disease or atrial arrhythmias following transplantation were studied. The Boston Scientific Constellation® basket catheter was used with St Jude EnSiteTM VelocityTM mapping system. Bipolar activation mapping was initially performed with basket array collapsed and positioned within the blood pool, away from the myocardium and then fully expanded to contact the endocardium with recording of bipolar EGMs.
Results: Mean voltage was lower for collapsed non contact bipolar EGM compared to contact EGMs (Voltage 0.9 vs 1.5 mV, $p<0.001$) Mean SNR was lower for non-contact compared to contact bipolar EGMs SNR 24.9 vs 29.7 dB, $p<0.001$). Impressive number of non-contact bipolar EGMs (89%) had acceptable signal-to-noise ratio (SNR ≥10). Of the seven tachycardias induced six were reentrant in nature and were identified by the non-contact bipolar EGMs. One focal atrial tachycardia, localized by non-contact bipoles was improperly located 1.5cm away from contact bipolar localization.
Conclusions: Non-contact Bipolar EGMs can be recorded with clinically acceptable signal to noise ratio, without specialized signal processing or inverse solution. Moreover using multielectrode array in non-contact bipolar mapping mode provides wavefront direction and rapid activation mapping for macro-reentrant rhythms. Together these findings suggest, there exists cavitary potentials that could be rapidly interrogated with array mapping to study wavefront propagation in adjacent myocardium.

AB31-02

NONINVASIVE EPICARDIAL AND ENDOCARDIAL MAPPING OF PREMATURE VENTRICULAR CONTRACTIONS

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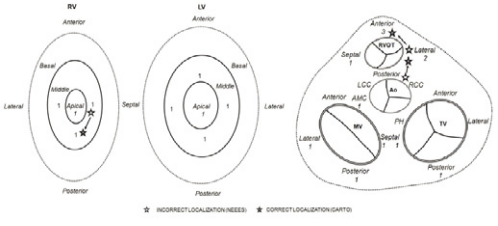
Introduction: We estimated the accuracy of a novel noninvasive epicardial and endocardial electrophysiology system (NEEES) for mapping of ectopic ventricular depolarizations.
Methods: The study enrolled 20 patients with monomorphic premature ventricular contractions (PVC) or ventricular tachycardia (VT). All patients underwent pre-procedural computed tomography or magnetic resonance imaging of the heart and torso. In the electrophysiology laboratory, up to 224 body-surface electrodes were connected to the NEEES (EP Solutions SA, Switzerland) followed by unipolar ECG recordings during episodes of PVC/VT. The body-surface ECG data was processed by the NEEES using its inverse-problem solution software in combination with anatomical data from the heart and torso. The earliest site of activation as denoted on the NEEES 3-dimensional heart model was compared with the PVC/VT origin using a 3-dimensional electroanatomical mapping system (Carto 3, Biosense Webster, US). The site of successful catheter ablation served as final confirmation.
Results: A total of 21 PVC/VT morphologies were analyzed and ablated. The chamber of interest was correctly diagnosed noninvasively in 20/21 (95%) PVC/VT cases. In 18/21 (86%) cases, the correct ventricular segment was diagnosed (Figure). Catheter ablation resulted in acute success in 19/20 (95%) patients, whereas 1 patient underwent successful surgical ablation. During 6 months of follow-up, 19/20 (95%) patients were free from recurrence off antiarrhythmic drugs.
Conclusions: The NEEES identifies the site of PVC/VT origin with sufficient accuracy.



AB31-03

CROSS MAPPING CAN IDENTIFY THE MECHANISMS OF ATRIAL TACHYCARDIA POST ATRIAL FIBRILLATION ABLATION

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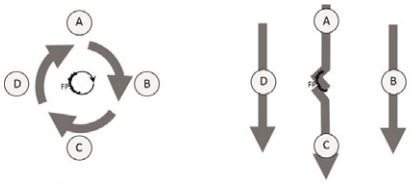
Introduction: Fractionated potentials (FP), covering nearly half of tachycardia cycle length (TCL), are often observed in atrial tachycardia (AT) post atrial fibrillation (AF). Some of these FPs present substrates for micro-reentrant AT (mAT), while others are bystander during AT. We investigated a method of cross mapping to identify the culprit FPs for mAT.
Methods: Mechanisms of ATs post AF were recognized by mapping. mAT was defined as a vortex-like conduction around a minuscule core (diameter<5mm) without any discernable obstacle. Cross mapping was performed: 1) Local activation times of 4 points (A, B, C and D, Figure) taken closely and evenly around a FP were measured. 2) The differences of local

activation time between A and C, B and D were calculated. 3) Time difference ratios (TDR), the difference of local activation time divided by TCL (AC/TCL and BD/TCL), were calculated.
Results: Totally 19 patients (60.5±9.1 years, 15 men) with successful ablation of ATs post AF ablation were enrolled. After 3-dimesional mapping, 14 FPs (group I) were indicated as substrate for mAT, while 20 FPs (group II) were bystanders for mAT episode. After cross mapping, the mean of AC/TCL and BD/TCL in group I was 54±23% and 41±25%, was 15±21% and 9±11%, respectively in group II. TDR ≥25% was used as the cut-off value for predicting mAT. The positive and negative predictive value was 71.4% and 100.0%, respectively, with sensitivity of 100.0% and specificity of 83.3%.
Conclusions: Cross mapping can differentiate culprit FPs from bystander FPs in mAT. Both cross over values of TDR ≥25% can be used as a key parameter.



Schematic diagram for the principle of cross mapping. Polyline represents an area with FP; Heavy arrow represents activation direction; A, B, C, and D represents a mapping point, respectively, FP: fractionated potential.

AB31-04

ACCURATE POP OCCURRENCE PREDICTION DURING RF ABLATION USING OCT

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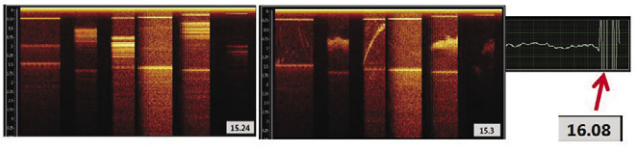
Introduction: Catheter ablation using RF energy is a validated therapy for most arrhythmias. Intra-tissular explosions (pops) during ablation are rare but may lead to fatal cardiac tamponades.
Methods: N/A.
Results: A regular TC catheter (BW) was used to create RF lesions on chicken hearts in a wet lab. An 8Fr prototype catheter equipped with optical coherence tomography (OCT) was placed next to the RF catheter to image the tissue in real time during RF delivery. A total of 60 RF lesions (20 at 30W, 50W and 60W) were conducted. 40 pops were observed (4@30W, 17@50W and 19@60W). Pops were always preceded by massive disruption of the OCT signal with loss of linearity as shown in the figure: at 15.24 sec, OCT is showing preserved linearity in all 6 OCT sensors while 0.06 sec after, at 15.3 s, linearity is lost in all OCT sensors. The pop was recorded on the audio track at 16.08 s, hence 0.78 s later. These linearity losses on OCT appeared 0.3 to 1.5 seconds (0.8±0.4) prior to the pop at 50W and 0 to 1.5 seconds (0.75±0.4) at 60W. This warning delay accounted for 5%±1% of the RF time preceding the appearance of the linearity loss. None of the lesions without pops were associated with these specific and massive OCT changes.
Conclusions: This developed 8Fr OCT prototype catheter was able to predict pops with excellent sensibility (98%) and specificity (100%). OCT embedded in irrigated tip ablation catheters could significantly increase safety.



AB31-05

HIGH-RESOLUTION MAPPING OF COMPLEX LEFT ATRIAL TACHYCARDIA: INITIAL EXPERIENCE WITH THE RHYTHMIA MAPPING SYSTEM

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Introduction: Rythmia is a new mapping system allowing rapid, high-resolution electroanatomical activation map with automated annotation algorithm. We sought to investigate its utility and acute efficacy in complex left atrial tachycardia (AT).
Methods: 49 consecutives patients (60±12 yo, 38 males, 14 (29%) SHD, LVEF: 52±15%, LA surface: 25±6 cm2) referred for complex AT were included. Most cases (58, 89%) were post-AF ablation AT. All AT were mapped using a 64 poles high-resolution catheter (ORIONTM) and Rhythmia mapping system. Precise mechanism of AT was defined based on the analysis of the atrial map and confirmed if needed by entrainment. The primary target for ablation was the earliest activation site in case of focal AT, the critical isthmus in case of reentrant AT if possible or the anatomic isthmus.
Results: A total of 83 AT were analyzed. Eighteen AT were excluded due to mechanical termination before the end of the mapping procedure. Left atrial high-resolution mapping was performed in 65 AT: 12490±5734 points/map; LA mapping time: 846±420sec. RA mapping was required in 14 cases (6625±3083points/map in 696±563sec). Accurate identification of the AT mechanism was possible in 61 cases (94%) with no or minimal manual reannotation (mean 0.5±2 points/patients). Mechanism of AT was focal in 12 (18%) cases, macro reentry in 38 (58%), localized reentry in 11 (17%) and undetermined in 4 (6%). Macro-reentrant AT were predominantly perimitral (n=15), then roof dependent (n=8), CTI-dependent (n=7), double loop (n=3) or other circuit (n=4). Termination of AT was obtained in 57 cases (88%) with a mean RF time of 324±762sec. High-density mapping was very efficient to characterize and identify the critical isthmus in localized reentry (termination rate: 100%, mean RF time: 123±208sec). The majority of failures were due to an inability to create a complete line of block across the macroreentrant circuit at the anatomic isthmus (mitral line (n=5); or roof line (n=1)). No procedural-related complications were noted.
Conclusions: In complex AT, the use of this new high resolution mapping system is feasible and allow accurate identification of the AT mechanism with high acute success rate. The potential advantages of this system compared to existing technologies remains to be determined.

ABSTRACT AB32:
VT Ablation: Timing of Intervention and Impact of Recurrence

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB32-01

PREVALENCE AND PREDICTORS OF EARLY MORTALITY FOLLOWING CATHETER ABLATION OFVENTRICULAR TACHYCARDIA IN PATIENTS WITH STRUCTURAL HEART DISEASE: RESULTS FROM THE INTERNATIONAL VT ABLATION CENTER COLLABORATIVE GROUP

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Introduction: In patients referred for radiofrequency catheter ablation (RFCA) of ventricular tachycardia (VT) in the setting of structural heart disease, early post-operative mortality has not been previously investigated. We evaluated the prevalence and predictors of patients experiencing early mortality following catheter ablation of scar-related VT.
Methods: Using logistic regression analysis we identified predictors of early mortality (within 30 days of the procedure) in 2,063 patients with structural heart disease (age 62±13 years, mean left ventricular ejection fraction [EF] 34±13%, 53% ischemic etiology) undergoing RFCA of VT in 12 international centers.
Results: Early mortality occurred in 97 (5%) patients, including 12 (0.6%) patients who died in the hospital following a major procedure-related complication (2 procedural deaths). At multivariable logistic regression analysis, left ventricular EF (odds ratio [OR] per % increase = 0.86, 95% confidence interval [CI] 0.79-0.94, P<0.001), New York Heart Association (NYHA) class (OR = 2.14, 95% CI 1.03 to 4.45, P=0.041), presentation with VT storm (>3 appropriate ICD interventions within 24-h, OR = 3.93, 95% CI 1.15-13.39, P=0.029) and longer procedural duration (OR per 30 min increase = 1.22, 95% CI 1.03-1.45, P=0.019) were independent predictors of early mortality.
No other clinical or procedural variables were found to be independently associated with early post-procedural mortality.
Conclusions: In a contemporary cohort of patients with scar-related VT undergoing RFCA, early (within 30 days) post-operative mortality occurs in 5% of cases. Low left ventricular EF, clinical presentation with VT storm and longer procedural duration are independent predictors of early mortality.

AB32-02

PROGNOSTIC IMPACT OF THE TIMING OF RECURRENCE OF INFARCT-RELATED VENTRICULAR TACHYCARDIA AFTER ABLATION

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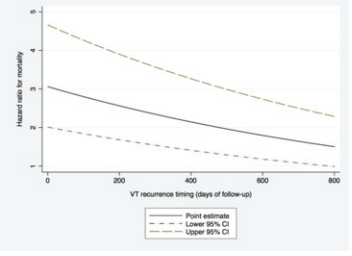
Introduction: Recurrence of ventricular tachycardia (VT) after VT ablation in patients with prior myocardial infarction is associated with adverse outcome. However, the impact of the timing of VT recurrence on mortality is unclear.
Methods: We analyzed data from a multicenter collaborative database of patients who underwent catheter ablation for infarct-related VT. Multivariate Cox regression analyses investigated the effect of the timing of VT recurrence on overall mortality. Adjustments were performed for variables that were different between the recurrence and "no recurrence" group at baseline and VT recurrence was modeled as a time-varying covariate.
Results: Overall, 1,004 patients were included (age 68±9.6 years, males 92%, mean follow-up 691 days). A total of 439 (44%) patients had a recurrence [161 (37%) within 1 month, 207 (47%) between 1 and 12 months and 71 (16%) after 12 months]. Mean time to VT recurrence was 178 days across all patients. In multivariate analysis, the mortality hazard ratio (95% confidence interval) for VT recurrence on day 1 relative to no recurrence was 3.06 (2.01-4.66). However, the magnitude of the HR associated with VT recurrence decreased significantly (p<0.001) as recurrence occurred later in the follow-up period (Figure). The respective mortality risk estimates for VT recurrence at 30 days, 6 months, 1 year, and 2 years were 2.98 (1.97-4.49), 2.60 (1.81-3.74), 2.21 (1.62-3.02), and 1.60 (1.24-2.06).
Conclusions: The timing of VT recurrence after ablation offers incremental prognostic information. Early recurrences portend high mortality risk but the magnitude of this effect decreases with later recurrences.



AB32-03

ARE THERE ANY CLINICAL AND SUBSTRATE DIFFERENCES AND RESPONSE TO CATHETER ABLATION IN PATIENTS WHO PRESENT WITH VENTRICULAR TACHYCARDIA (VT) STORM VERSUS THOSE WHO DO NOT?

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Introduction: It is unclear why some pts present with VT storm whereas others do not. In patients with structural heart disease, we sought to compare the clinical & substrate characteristics & response to catheter ablation among patients who presented with VT storm versus those who did not.
Methods: 919 consecutive patients with ischemic (ICM; n=552; storm 213) or non-ischemic cardiomyopathy (NICM: n=367; storm 120) with sustained monomorphic VT referred for catheter ablation were included. Patients were divided into those who presented with VT storm (>3 episodes of VT/24 hours) vs. those who did not.
Results: In ICM, storm pts had significantly lower EF, shorter elapsed time since last infarct, slower VTs, greater number of scarred LV segments, & higher incidence of septal, apical & anterior LV scar compared to non-storm pts (all P<0.05; P=0.07 anterior scar). Acute procedural success did not differ (non-inducibility 59% vs. 56%, P=0.6), but non-RFA ablation (transcoronary alcohol/surgical cryoablation) was more frequently required in storm pts (8% vs. 4%, P=0.03). Unadjusted VT-free survival was lower in storm vs. non-storm pTS (1y: 44% vs. 53%, P=0.04) but overall survival was not (3y: 60% vs. 69%, P=0.09). In NICM, pts with storm were older, had lower EF, larger LV end diastolic diameters, slower VTs, & higher incidence of lateral LV scar compared to non-storm pts (all P<0.05). Acute procedural success did not differ (non-inducibility 47% vs. 51%, P=0.6) but non-RFA ablation was more frequently required in storm pts (14% vs. 6%, P=0.02). Unadjusted VT-free survival was lower in storm vs. non-storm patients (1y: 24% vs. 53%, P<0.001) as was overall survival (3 y: 69% vs. 83%, P=0.03). After multivariable adjustment, VT storm was not an independent predictor of survival in ICM (hazard ratio [HR] 1.1, P=0.8) nor NICM pts (HR 1.2, P=0.4) but age (P<0.001) and EF (P<0.001) were powerful predictors in both groups.
Conclusions: There are fundamental clinical & substrate differences in pts with structural heart disease who present with VT storm vs those who do not. Acute procedural success and adjusted-long term survival after catheter ablation appear to be similar regardless of storm presentation or not.

AB32-05

SAFETY, LONG-TERM OUTCOMES AND PREDICTORS OF RECURRENCE AFTER FIRST-LINE COMBINED ENDOEPICARDIAL VENTRICULAR TACHYCARDIA SUBSTRATE ABLATION IN ARRHYTHMOGENIC CARDIOMYOPATHY. IMPACT OF ARRHYTHMIC SUBSTRATE DISTRIBUTION PATTERN. A PROSPECTIVE MULTCENTER STUDY

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Introduction: First-line endoepicardial ventricular tachycardia (VT) ablation has been proposed for patients with arrhythmogenic cardiomyopathy (AC). The aim was to assess safety, outcomes and predictors of recurrence.
Methods: Forty-one consecutive patients 12 with left ventricle (LV) involvement, 7 left-dominant underwent first-line endo-epicardial VT substrate ablation. Standard bipolar and unipolar thresholds were used to define low voltage areas (LVA). Arrhythmogenic substrate area (ASA) was defined as the area containing electrograms with delayed components. Implantable cardioverter defibrillator interrogations were evaluated for VT recurrence.
Results: Epicardial LVA was larger in all cases (102.5±78.6 vs 19.3±24.4 cm2; p<0.001). Consistent with an epicardium-to-endocardium arrhythmogenic substrate progression pattern, epicardial ASA was negatively correlated with bipolar endocardial LVA (r=-0.368; p=0.035) and with endocardial bipolar/unipolar-LVA (Bi/Uni-LVA) ratio (r=-0.38; p=0.037). Patients showing an epicardial ASA<10 cm2 were classified as advanced stage AC. Advanced stage AC patients required less epicardial (8.4±5.8 vs 25.3±16; p=0.045) and more endocardial (16.5±8.6 vs 7.5±8.2; p=0.047) radiofrequency applications. One patient with advanced AC died of cardiac tamponade after epicardial puncture. A Bi/Uni-LVA ratio >0.23 predicted an epicardial ASA10 cm2 (100% sensitivity, 84% specificity). After 32.2±21.8 months 11 patients had VT recurrences. Left-dominant AC was associated with an increased risk of recurrence (HR=3.41 [1.1-11.2], p=0.044; log-rank p=0.021).
Conclusions: First-line endoepicardial VT substrate ablation achieves good long-term results in AC. Left-dominant AC is associated with an increased risk of recurrence. The Bi/Uni-LVA ratio identifies patients at advanced stages with limited epicardial arrhythmogenic substrate in whom the indication of epicardial approach should be more cautiously assessed.

AB32-06

CARDIAC SYMPATHETIC DENERVATION FOR INTRACTABLE VENTRICULAR ARRHYTHMIAS IN CHAGAS DISEASE: AUTONOMIC INTERVENTION FOR AN AUTONOMIC DISORDER

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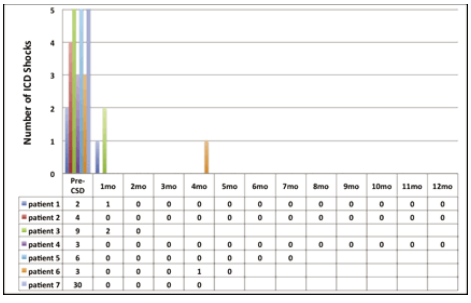
Introduction: Autonomic modulation is a valuable therapeutic option for the management of ventricular arrhythmias. Bilateral cardiac sympathetic denervation (BCSD) has shown promising results in acute, intermediate and long-term management of

polymorphic and monomorphic ventricular tachycardia (VT) in patients with structural heart disease. Cardiomyopathy (CM) due to Chagas disease (CD), and associated VT, is thought to be in large part due to autonomic neuronal destruction and dysfunction. Whether BCSD is a safe and effective treatment modality in this patient population has not been explored.
Methods: Retrospective analysis of data from patients with Chagasic CM who underwent BCSD between 2009 and 2015 at two sites, in the US and Colombia, was performed.
Results: Of seventy-five patients who underwent BCSD for VT storm/refractory VT in the setting of CM, 7 patients had CD as the etiology of CM. These patients were (Median [range]) 51 (46-60] years old, and had ejection fraction 35 [10-45]%. Country of origin was Colombia in 3/7, Mexico 3/7, and El Salvador 1/7. Follow-up was 7 [1-46] months. All patients had failed amiodarone and either had underwent unsuccessful ablation or were not candidates for ablation. The median number of ICD shocks 1 month prior to BCSD was 4 [2-30] and decreased to 0 [0-2] in available follow-up after BCSD, with only one patient having recurrent sustained VT after 1 month post-BCSD (Figure).
Conclusions: In Chagasic CM patients presenting with VT storm or VT refractory to antiarrhythmic therapy and/or catheter ablation, early evidence suggests BCSD reduces ICD shocks and may represent a valuable treatment option.



	Pre-CSD	1mo	2mo	3mo	4mo	5mo	6mo	7mo	8mo	9mo	10mo	11mo	12mo
patient 1	2	1	0	0	0	0	0	0	0	0	0	0	0
patient 2	4	0	0	0	0	0	0	0	0	0	0	0	0
patient 3	9	2	0										
patient 4	3	0	0	0	0	0	0	0	0	0	0	0	0
patient 5	6	0	0	0	0	0	0	0					
patient 6	3	0	0	0	1	0							
patient 7	30	0	0	0	0								

ABSTRACT PLUS AB33:
New Insights Into AF Mechanisms

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB33-01

THREE-DIMENSIONAL WAVEMAPPING OF HUMAN PERSISTENT ATRIAL FIBRILLATION

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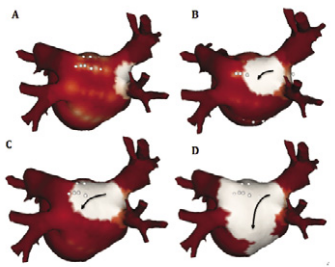
Introduction: The mechanism of persistent atrial fibrillation (perAF) remains uncertain. We sought to determine the prevalence of focal drivers and rotors during human perAF using novel 3D wavemapping technique that projects local activation onto patient specific 3D geometry.
Methods: Left atrial mapping was performed during AF in 12 patients using the multi-electrode basket catheter. Continuous one-minute AF recordings were analyzed offline using customized signal processing software (CEPAS, Curotech). The local activation at each electrode site was determined using automatic annotation with manual correction to the peak of the bipolar electrogram. Activation data was projected onto 3D surface geometry using novel wavemapping software. Activation patterns were classified into i) wavefronts (single or multiple) ii) rotors (≥ 2 rotations of 360°) iii) or focal sources with radial spread. In addition, the spatial distribution and origin of wavefronts was determined.
Results: Over 5000 activation patterns were analyzed. Mean AF cycle length was 185±107ms. Activation patterns were highly dynamic and heterogeneous. The most common patterns were i) single wavefronts (75.9%), ii) two simultaneous wavefronts 6.4%, iii) transient focal activations in 17.7%. No sustained focal activity or rotors were seen. In majority of maps (54.2%), the wavefronts appeared to originate from the anterior wall. Focal activity most commonly arose from the posterior wall adjacent to the left superior pulmonary veins.
Conclusions: Activation patterns in perAF are highly heterogeneous with single wavefronts appearing to be dominant subtype. No rotors or sustained focal activity were observed.



Panel A. Activation wavefront appears to originate from right inferior pulmonary vein. **Panel B and Panel C.** Wavefront propagates towards the left sided pulmonary veins. **Panel D.** Activation wavefront then propagates towards the floor of the left atrium.

AB33-02

RATE-DEPENDENT SHORTENING OF EFFECTIVE REFRACTORY PERIOD WITH CONDUCTION SLOWING IN LEFT PULMONARY VEIN INCREASES VULNERABILITY TO PAROXYSMAL ATRIAL FIBRILLATION

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Introduction: Premature atrial complex (PAC) originating from pulmonary veins (PVs) triggers AF. We have reported that intra-PV extra stimulation, mimicking PAC, can provoke AF (HRS 2015); AF was more frequently induced in paroxysmal AF patients (pAF) than in persistent AF patients, suggesting that PV electrophysiological properties are responsible for vulnerability in pAF. We examined if PV responses to extra stimulation can evaluate PV-dependent electrophysiological substrate and estimate PV isolation (PVI) efficacy in pAF.
Methods: In 50 pAF patients undergoing PVI, single extra

stimulation was applied to the left- and right-PVs (LPV and RPV), coronary sinus (LA), and RA. Electrical impulses at twice the pacing threshold were delivered at basic cycle lengths (BCLs) of 600ms and 400ms, followed by extra stimulation in 10-ms decrements. AF inducibility and effective refractory period (ERP) were evaluated before PVI. Conduction time was measured and then conduction velocity (CV) was calculated (catheter electrode distance divided by conduction time). The 1-year AF-free survival rate was assessed using Kaplan-Meier analysis.
Results: Single extra stimulation provoked AF in 68% patients with pAF: LPV showed the highest AF inducibility (LPV: 60%, RPV: 22%, both PVs: 12%, RA: 6%, $p<0.05$). At a longer BCL (600ms), ERPs in the LPV, RPV, LA, and RA were unchanged between AF-inducible group (AF[+]) and AF-non-inducible group (AF[-]). However, at a shorter BCL (400ms), ERP in the LPV significantly decreased in AF[+] vs. AF[-] by 12%* (*$p<0.05$) whereas LPV-LA ERP gradient increased in AF[+] by 136%*. CVs in the LPV at BCLs of 600ms and 400ms decreased in AF[+] vs. AF[-] by 23%* and 24%*, respectively. In echocardiography, LA diameter (an index of structural remodeling) was unchanged between AF[+] and AF[-]. At 1-year after PVI, AF[+] showed a higher AF-free survival rate than AF[-] (95% vs. 64%, log-rank=5.368*).
Conclusions: AF[+] had rate-dependently shorter LPV ERP and greater LPV-LA ERP heterogeneity along with slower LPV CVs than AF[-], at least partly contributing to increased LPV-dependent vulnerability in AF[+]. PVI can eliminate these substrate and thus may be more efficient in AF[+] than in AF[-], likely causing its higher AF-free survival rate.

AB33-03

FIRST-IN-MAN CORRELATION OF NON-INVASIVE AND INVASIVE PHASE MAPPING OF ATRIAL FIBRILLATION

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Introduction: The novel non-invasive epicardial and endocardial electrophysiology system (NEEES) allows for reconstruction of local cardiac unipolar electrograms (EGs) derived from body-surface potentials. The current study assessed phase approaches for non-invasive mapping of atrial fibrillation (AF) applying the NEEES as compared to invasive electroanatomical mapping using the CARTO 3 3D-navigation system in conjunction with a PentaRay Nav catheter.
Methods: Patients with persistent AF underwent cardiac magnetic resonance imaging followed by NEEES (EP solutions SA, Yverdon-les-Bains, Switzerland)-based analysis and phase mapping with localization of electrical rotors. The obtained non-invasive phase mapping data were compared to electroanatomical mapping applying the CARTO 3 3D-mapping system and the PentaRay Nav catheter (Biosense Webster, Diamond Bar, US). Catheter-derived EGs were processed using the same phase mapping algorithm as for non-invasive analysis.
Results: Six consecutive patients with persistent AF (6 male, 59 [45;74] years, LA-diameter 49±5 mm, AF-duration 5 [1;7] months) were analyzed. Mean number of rotors/patient detected by NEEES was 36 (30;45); left atrial 25 (17;38), right atrial 9 (5;15). Noninvasively identified rotors demonstrated spatial aggregation at few dominant sites: >80% aggregated in two (5 patients) or three (1 patient) sites. Rotor occurrence rate during the observation period (1/sec) obtained by Pentaray and by NEEES at dominant aggregation sites demonstrated significant contingency (Pearson's χ^2test, $p<0.05$). Noninvasively and invasively detected rotors demonstrated comparable characteristics (number of 360° rotations: 1.2 [1; 3] by NEEES vs. 1.2 [1; 3] by Pentaray; clockwise rotors: 45% [36%; 57%] by NEEES vs. 46% [20%; 60%] by Pentaray; cycle length: 161 [147;176] ms by NEEES vs. 160 [141;172] ms by Pentaray.
Conclusions: The current study revealed significant correlation of non-invasively and invasively identified rotors in patients with persistent AF.

AB33-04

FURTHER CHARACTERIZATION OF FOCI DURING PERSISTENT AND LONG-STANDING PERSISTENT ATRIAL FIBRILLATION IN PATIENTS - STUDIES USING HIGH DENSITY (510-512 ELECTRODES) BI-ATRIAL EPICARDIAL MAPPING

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Introduction: One demonstrated mechanism of persistent and long-standing persistent (LSP) atrial fibrillation (AF) is that it is due to multiple foci (sustained and/or intermittent) of different cycle lengths (CLs) which activate the atria, contributing to the maintenance of AF. The purpose of this study was to quantify characteristics of sustained and intermittent foci identified during high density mapping of AF in patients with persistent and LSP AF
Methods: We recorded the sequence of atrial activation during 11 episodes of AF in 11 patients with persistent and LSP AF (1 month - 9 years duration) at open heart surgery. During AF, electrograms (AEGs) were simultaneously recorded from both atria for 1 - 5 minutes from 510-512 epicardial electrodes, arranged in bipolar pairs, along with ECG lead II. From each patient, analysis of consecutive 32 secs of identified sustained and/or intermittent foci was performed. Bipolar AEGs at focal sites were subjected to CL variability detection analysis to determine the mean CL and CL variation (% = standard deviation / mean CL).
Results: During persistent and LSP AF, multiple foci (sustained [range 1 - 2] and/or intermittent [range 1 - 3]) of different CLs were present in both atria in all patients. A total of 8 sustained foci (mean CL 170±19 ms; range 142-200 ms; duration 32 s) and 21 intermittent foci (mean CL 176±18 ms; range 143-211 ms) were identified in all patients. Temporal CL behavior of sustained foci varied (6/8, maximum change of mean CL: 20 ms), but the CL variation for each sustained focus was always ≤ 10%. The temporal behavior of intermittent foci, i.e., the duration of individual episodes, was variable: focal bursts lasted 0.2 - 19.7 s, and the total duration per each intermittent focus ranged from 5 - 30.5 s. Periods of no focal activation were due to a spontaneous pause (13/21) or activation of the focal site by wave fronts originating from another focus or a breakthrough site (14/21).
Conclusions: During persistent and LSP AF, 1) each sustained focus manifested variable CLs over time, but CL variability was always less than 10%; 2) intermittent foci manifested variability

in both CLs and periods of activity; 3) spontaneous pauses or activation from other wave fronts explained the intermittency of the intermittent foci.

AB33-05

IDENTIFCATION MORPHOLOGICAL REPETITIVENESS OF WAVEFORMS PATTERNS IN FRACTIONATED ELECTROGRAMS DURING PERSISTENT ATRIAL FIBRILLATION

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Introduction: Targeting the sites with continuous complex fractionated atrial eletrograms (CFEs) in combination of high level of electrogram morphology similarity during substrate modification is more likely to terminate atrial fibrillation (AF). This study applied two waveform analyses to explore the morphological repetitiveness of waveforms and how those patterns clustered throughout the time to reveal hidden structure of seemingly chaotic fibrillatory electrograms.
Methods: 100 AF patients who underwent catheter ablation were included and substrate ablation was performed on 79 patients. Point-by-point time-domain bipolar signals (6 seconds) were acquired for recurrence plots (beat-to-beat sequential plot of morphology) with nonlinear-based waveform similarity analysis. The fibrillation signals were acquired and analyzed using the similarity index (SI) and the recurrence plots. CFEs were targeted with the objective of termination.
Results: A total of 9,558 fibrillatory electrograms were analyzed in this study (139 ± 30 sites per patient in the LA). Procedural termination was observed in 39% and long-term sinus rhythm maintenance in 67% of the patients. In addition to the higher waveform similarity, indicated by SI, at targeted CFEs , clustering of repetitive waveforms (3.37±0.68 vs 3.29±0.75 waves per cluster; p< 0.03) with higher periodicity were also found in patients with procedural AF termination or in AF recurrence-free patients (Fig).
Conclusions: Utilizing recurrence patterns method to analyze complex fraction electrograms, it was discovered that sites with rapid activation of periodically repetitive morphology patterns may be critical for sustaining AF.

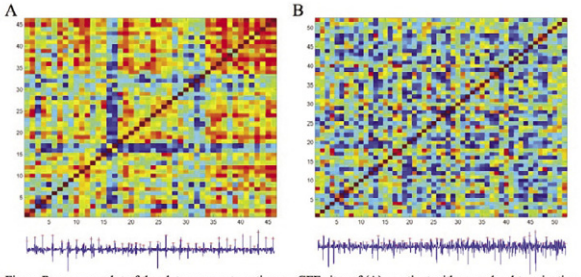


Figure Recurrence plot of the eletrograms at continuous CFE sites of (A) a patient with procedural termination and (B) a non-termination paticnt

ABSTRACT AB34:
Novel Mapping Approaches for Ventricular Arrhythmia

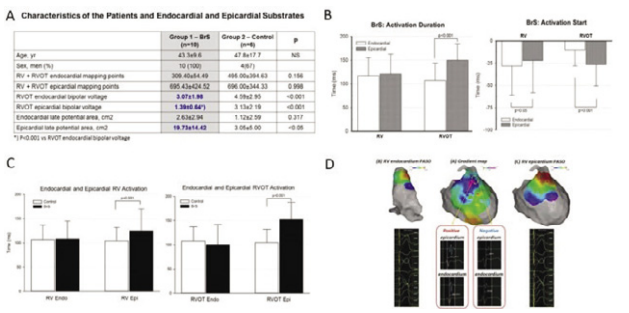
Friday, May 6, 2016
1:30 PM - 3:00 PM

AB34-01

CONFLUENCE ABNORMAL ELECTROGRAMS AND HETEROGENEOUS PLANAR ACTIVITY PROPAGATION IN THE EPICARDIUM OF ANTERIOR FREE WALL OF RIGHT VENTRICULAR OUTFLOW TRACT IN BRUGADA SYNDROME

Fa-Po Chung, MD, Yenn-Jiang Lin, MD, Shih-Lin Chang, MD, Li-Wei Lo, MD, Yu-feng Hu, MD, Ta-Chuan Tuan, MD, Tze-Fan Chao, MD, Jo-nan Liao, MD, Chin-Yu Lin, MD and Shih-Ann Chen, MD. Taipei Veterans General Hospital, Taipei, Taiwan, Taipei Veterans General Hospital/National Yang-Ming University, Taipei, Taiwan

Introduction: Transmural discrepancy contributes to the phenotype and arrhythmogenicity in Brugada syndrome (BrS) The reginal differences of transmural activation pattern in identification of optimal substrates responsible for VT/VF in BrS have not been delineated clearly.
Methods: A total of 10 BrS patients and 6 patients with idiopathic VPC/VT as control were studied. Detailed endocardial and corresponding epicardial mapping were extracted for comparison.
Results: The epicardial voltage within RVOT in BrS was lower than corresponding endocardial voltage (P<0.001) and those in control patients (P<0.001). The epicardial electrogram duration in BrS was significantly longer than corresponding endocardial electrogram for both RV (P<0.001) and RVOT (P<0.001). However, endocardial RV breakout occurred earlier than those within epicardium (28.2±32.5 ms vs. 22.0±36.2 ms, P<0.05), while reverse activation breakout from epicardium to endocardium was observed within RVOT (9.9±18.1 ms and 26.5±24.2, P<0.001). Moreover, area with maximal activation gradient (59±6 ms) was compatible with the exit sites of VT in all patients (r= 0.9±0.1).
Conclusions: The presence of confluence of abnormal electrograms in the epicardium of anterior free wall of RVOT and the heterogeneous planar activity propagation in the Brugada patients indicated the potential mechanism responsible for the ventricular arrhythmogenesis, which also provided the optimal ablation target.



AB34-02

NONINVASIVE HIGH-RESOLUTION EP MAPPING IN POST-MI PATIENTS: THE ELECTROPHYSIOLOGICAL SUBSTRATE IN RELATION TO VENTRICULAR ARRHYTHMIAS

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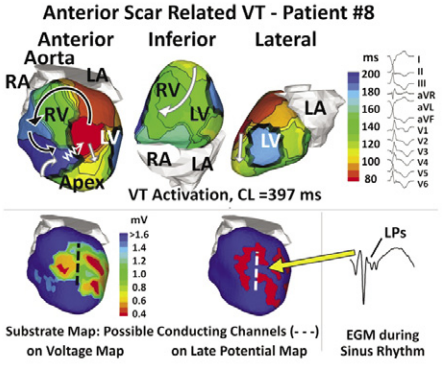
Introduction: Myocardial infarction (MI) can provide the substrate for ventricular tachycardia (VT). The study aim was to map noninvasively the electrophysiological (EP) scar substrate in post-MI patients and identify its relationship to reentry circuits during VT.
Methods: Noninvasive high-resolution epicardial mapping with Electrocardiographic Imaging (ECGI) was performed in 17 patients with infarct-related myocardial scar and clinical VT. Abnormal EP scar substrate was determined during sinus rhythm based on electrogram amplitude, fractionation and the presence of late potentials (LPs). High-resolution mapping within the scar provided detailed spatial EP properties of the heterogeneous substrate. The VT activation pattern was mapped and correlated with the EP substrate to identify components of the reentry circuit.
Results: The epicardial EP substrate associated with MI was characterized by low-voltage and fractionated electrograms, the presence of LPs, and altered sinus rhythm activation pattern. Repolarization abnormalities were not present, indicating that the mechanistic basis for conduction block and VT is structure-based abnormal propagation through the scar substrate. VT was mapped in 8 patients; the reentry circuits were closely related to the EP substrate, aligning with possible conducting channels of relatively preserved voltage and presence of LPs within the scar.
Conclusions: ECGI noninvasively identified the EP scar substrate that underlies abnormal conduction in post-MI patients. It identified regions within the scar that aligned with critical elements of the reentry circuit during VT.



Example: Double Loop Reentry. The ECGI-mapped VT is shown (top) together with the Substrate map (bottom). The VT common pathway is through the scar, possibly through a region of relatively higher voltage that supports LPs.

AB34-03

HIGH-DENSITY PACEMAP-GUIDED ABLATION OF VENTRICULAR TACHYCARDIA IN THE SETTING OF NONISCHEMIC CARDIOMYOPATHY

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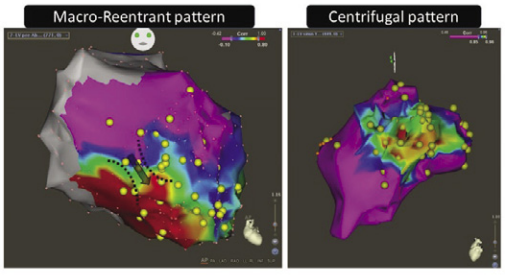
Introduction: It has been recently reported that correlation score map generated by multiple pacemap within and around scar may identify critical isthmus of well-tolerated ventricular tachycardias (VTs) in patients with ischemic cardiomyopathy (ICM). However, little is known about the feasibility and efficacy of high-density pacemap approach to ablation of scar-mediated VTs in patients with nonischemic cardiomyopathy (NICM).
Methods: We studied 37 correlation score maps (22 in ICM, 15 in NICM, 31 [84%] for unmappable VTs) that were obtained in 13 patients (7 ICM, 6 NICM) undergoing mapping/ablation of scar-mediated VTs. Correlation score map, which represents color-code correlating to the percentage of matching between the 12-lead ECG during VTs and that during pacemap, was created using CARTO3 PaSo module.
Results: The types of correlation score maps were classified into 2 patterns: (1) centrifugal pattern, and (2) macro-reentrant pattern representing abrupt change in color-coded sequence from poorest score region (isthmus entrance part) to best score region (isthmus exit part)(Figure). Most of VTs in patients with ICM (16/22 maps [73%]) showed macro-reentrant pattern. Ablation of VT critical isthmus guided by macro-reentrant pattern rendered the VT non-inducible in all patients. On the contrary, 73% of VTs in patients with NICM showed centrifugal pattern, suggesting intramural location of the critical isthmus. During follow-up period, VT recurrence rate was higher in patients with NICM than ICM (67% vs. 29%).
Conclusions: Although high-density pacemap approach is feasible in both ICM and NICM patients, the efficacy of this approach may be limited in patients with NICM.



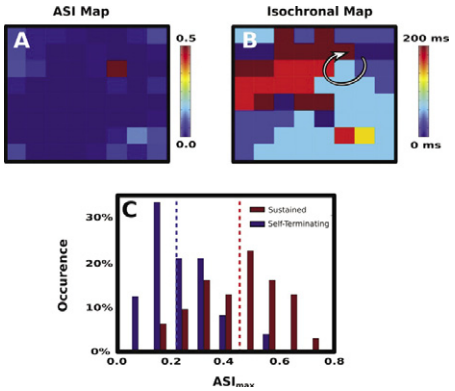
AB34-04

ANOMALOUS SYNCHRONY SUGGESTS HUMAN VENTRICULAR FIBRILLATION IS SOURCE-DRIVEN RATHER THAN DISORGANIZED

Wouter-Jan Rappel, PhD, David Vidmar, MSc, Amir A. Schricker, MD, Gordon Ho, MD, Christopher Villongco, PhD, Junaid Zaman, MD, Sanjiv Narayan, MD, PhD and David E. Krummen, MD. University of California, San Diego, La Jolla, CA, UC San Diego Medical Center, San Diego, CA, Stanford University, Stanford, CA, University of California, San Diego, San Diego, CA

Introduction: An increasing body of work supports the role of spiral reentry in maintaining ventricular fibrillation (VF), but current methods rely on manual evaluation of computed phase

movies. We hypothesized that automated synchronization analysis may identify spiral tip areas during VF corresponding to VF-maintaining sites.
Methods: In consecutive patients presenting for ventricular arrhythmia ablation, VF was induced and recorded with 64-electrode basket catheters during defibrillator charging. Electrogram phase was computed from activation times, and synchrony was computed for each pair of electrodes. Areas of elevated Anomalous Synchrony Index (ASI), identifying regions of tissue which are dynamically out-of-step with neighboring synchronous tissue, were calculated.
Results: In 29 patients (16 with LVEF < 50%, age 65±10 y), areas of elevated ASI (greater than 0.25) occurred in 7 out of 13 self-terminating episodes, and 16 out of 16 sustained episodes (p=0.01). Fig. A shows an area of elevated ASI = 0.66 in a patient in whom targeted ablation of the spiral wave tip area (Fig. B) prevented subsequent VF initiation. Median ASImax was lower across self-terminating episodes (0.22) than sustained episodes (0.45, p=0.01, Fig. C).
Conclusions: A quantitative examination of phase synchrony identifies sources maintaining human VF. Future work should further investigate targeted intervention at sites showing elevated ASI to reduce VF susceptibility.



AB34-05

RIPPLE MAPPING THE DIASTOLIC PATHWAY OF POST INFARCT VENTRICULAR TACHYCARDIA REVEALS COMPLEX ACTIVATION WITHIN THE SCAR SUBSTRATE

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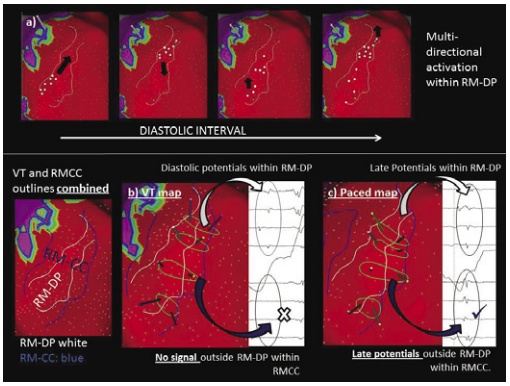
Introduction: Channels of surviving myocardium within infarct scar are critical to the re-entrant VT circuit. Ripple Mapping (RM) follows local activation through scar by displaying every electrogram deflection as a dynamic bar over a bipolar voltage map. We used RM to investigate the relationship between the diastolic pathway (RM-DP) in VT with conducting channels (RM-CC) in sinus/paced rhythm.
Methods: High density bipolar LV endocardial electrograms were collected using CARTO3v4 in sinus/paced rhythm as well as sustained monomorphic VT. RM-CC and VT activation were compared.
Results: RMs of 1205±1026 EGMs in VT and 846±740 EGMs in sinus rhythm/pacing from 3 scars (75±9cm2) were compared as part of a 15pt study ablating RMCCs. All visible parts of the RM-DP (length 61±17mm, area 5±0.3cm2, 0.27±0.18mV EGMs activating over 46% of the TCL) co-located within the RM-CCs (length 60±23mm, area 5.4±3cm2, 0.21±0.17mV local EGM). Ablation within each RM-DP interrupted the VT circuit. Activation within RM-DPs was multi-directional (a) and consistent between consecutive cycles. The lines of block bordering the RM-DPs were formed of myocardium with no signal during VT but of conducting myocardium during sinus rhythm (0.22±0.1mV) indicating functional block (b-c). Importantly, these areas of functional block were within the RM-CC edges (20±13% of RMCC area) and not at the infarct-border zone as defined by bipolar voltage mapping.
Conclusions: The diastolic pathway in VT appears to co-locate with RM-CCs identified in post infarct scar. RM-CC borders are the location of stable, functional lines of block despite multi-directional activation within the diastolic pathway.



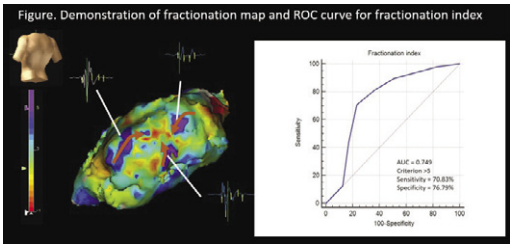
AB34-06

A NOVEL STRATEGY OF USING FRACTIONATION OF ELECTROGRAM OBTAINED DURING SINUS RHYTHM IN CATHETER ABLATION OF SUBSTRATE VENTRICULAR TACHYCARDIA

Yuan Hung, MD, Yenn-Jiang Lin, MD, Fa-Po Chung, MD, Shih-Lin Chang, MD, Li-Wei Lo, MD, Yu-feng Hu, MD and Shih-Ann Chen, MD. Tri-Service General Hospital, Taipei City, Taiwan, Taipei Veterans General Hospital, Taipei, Taiwan, Taipei Veteran General Hospital, Taipei, Taiwan, Taipei Veterans General Hospital/National Yang-Ming University, Taipei, Taiwan

Introduction: Substrate ablation toward VT isthmus could decrease the recurrent VT or death and mapping to identify VT circuit during sinus rhythm (SR) is difficult. We aimed to identify the VT isthmus with a novel fractionation algorithm during SR.
Methods: Ten patients (age 53 ± 18 years, 8 males) with symptomatic substrate VTs/VPCs (5 ischemic VT, 3 non-ischemic cardiomyopathy, and 2 arrhythmogenic cardiomyopathy) were enrolled and total 10051 mapping points (1008 ± 701 points per patient) were analyzed with Velocity™ Precision 2.0 Automap™ Software, St. Jude medical, USA. All collecting points were met the settings of SR fractionation algorithm as below: (1) the SR ECG morphology with ≥ 80% similarity scores, and (2) each fractionated electrogram (EGM) met the criteria of minimal complex width of 10 ms and minimal 15 ms in refractory period. All VT isthmus identified were rechecked by 3 independent observers.
Results: Thirteen clinical VTs/VPCs were induced and one non-clinical VT/VPC was found. The sensitivity and specificity of fractionation index to identify VT isthmus were 70.8% and 76.8% (AUC = 0.749, optimal cut-off value of fractionation index ≥5). Under the setting of fractionation index of 5, total 11 isthmuses were identified with the SR fractionation maps, which consisted of 84.6 % clinical VT isthmus. All the isthmus were within bipolar low voltage zone (voltage < 1.5mV) (Figure).

Conclusions: Using novel commercialized algorithm for construction of fractionation maps to identify VT isthmus is a valuable method and provide feasible information for substrate mapping and ablation in substrate VTs.



ABSTRACT AB35: Atrial Fibrillation, Thromboembolism, and the Left Atrial Appendage

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB35-01

IS ORAL ANTICOAGULATION NECESSARY IN YOUNG ATRIAL FIBRILLATION PATIENTS (20-49 YEARS) WITH A CHA2DS2-VASC SCORE OF 1 (MALES) OR 2 (FEMALES)?

Yuan Hung, MD, Tze-Fan Chao, MD and Shih-Ann Chen, MD. Tri-service General Hospital, Taipei City, Taiwan, Taipei Veterans General Hospital, Taipei, Taiwan, Taipei Veterans General Hospital/National Yang-Ming University, Taipei, Taiwan

Introduction: Recent studies have demonstrated that oral anticoagulants (OACs) should be considered for patients with atrial fibrillation (AF) with 1 additional risk factor of ischemic stroke beyond sex (CHA2DS2-VASc score of 1 for males and 2 for females). Since age is an important determinant of ischemic stroke, the strategy for stroke prevention may be different for these patients in different age strata.
Methods: This study used the "National Health Insurance Research Database" in Taiwan. A total of 7,374 AF males with a CHA2DS2-VASc score of 1 and 4,461 AF females with a CHA2DS2-VASc score of 2 without use of any anti-platelet or anti-coagulant agent were identified as the study population. Study patients were stratified into three groups by age (aged 20-49, 50-64, and 65-74 years). The annual risks of ischemic stroke were analyzed and calcualted for patients with specific covariates composing the score in different age strata. The threshold for the initiation of anticoagulation for stroke prevention was set at a stroke rate of 1.7%/year for warfarin and 0.9%/year for non-vitamin K antagonist OACs (NOACs).
Results: For AF males, the annual risks of ischemic stroke for patients aged 20-49, 50-64 and 65-74 years were 1.3%, 3.13%, and 3.68%, respectively. For male patients aged 20-49 years, the stroke risk was lowest for those with hypertension (0.94%/year), and highest for those with congestive heart failure (1.71%/year). For AF females, the annual risks of ischemic stroke for patients aged 20-49, 50-64 and 65-74 years were 1.4%, 2.64%, and 3.46%, respectively. For female patients aged 20-49 years, the stroke risk was lowest for those with hypertension (1.11%), and highest for those with congestive heart failure (1.67%).
Conclusions: Even for young AF patients with 1 additional stroke risk factor beyond gender, the annual risk of ischemic stroke have exceeded the threshold for the initiation of NOACs for stroke prevention. However, the annual risk of ischemic stroke for AF patients aged 20-49 years with hypertension only was around 0.94-1.11% which was just slightly higher than the "tipping point" for using NOACs (0.9% per year). Therefore, how to treat these patients should be based on shared decision-making with patients to discuss about the risks and benefits of OACs.

AB35-02

ADVANCED ELECTROANATOMICAL REMODELING OF LEFT ATRIUM AND CONTRACTILE DYSFUNCTION OF LEFT ATRIAL APPENDAGE ARE THE PREDOMINANT MECHANISMS OF STROKE IN WOMEN IN ATRIAL FIBRILLATION

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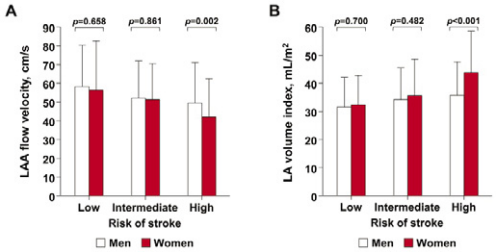
Introduction: The risk of stroke imposed by atrial fibrillation (AF) is significantly greater in women than men; however, the mechanism behind the observed differences remains elusive. We hypothesized that left atrial (LA) remodeling and poor contractile function of LA appendage (LAA) generate stroke more predominantly in women than men among AF patients.
Methods: A total of 634 AF patients (233 women and age- and AF type-matched 401 men, 62.2±9.5 years old, 71.6% paroxysmal AF) who underwent AF catheter ablation were enrolled in this retrospective observational study. Gender differences of LA volume index (LAVI), LAA emptying flow velocity (FV) and LA voltage were analyzed in low (0 for men, 1 for women), intermediate (1 for men, 2 for women) and high (≥2 for men, ≥3 for women) risk groups, divided based on their CHA2DS2-VASc scores.
Results: 1. LAA-FV was more significantly reduced in women with a high stroke risk than in men of the same risk (p=0.002). 2. Women showed greater LAVI than their male counterpart in the high risk group (p<0.001). 3. Women showed lower LA and LAA voltage than men in the high risk groups (p<0.001). 4. LAVI (OR 1.051, 95% CI 1.014-1.091, p=0.007) and left ventricular ejection fraction (OR 0.929, 95% CI 0.881-0.979, p=0.006) were independently associated with the history of stroke in women but not in men.
Conclusions: More extensive LA remodeling and deterioration in LAA function were noted in women with high risk of stroke in AF, and advanced electroanatomical remodeling was predictive of stroke in women but not in men.



AB35-03

RISK OF STROKE AND BLEEDING IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY AND ATRIAL FIBRILLATION TREATED WITH NON-VITAMIN K ANTAGONIST ORAL ANTICOAGULANTS OR WARFARIN

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Introduction: Hypertrophic cardiomyopathy (HCM) affects more than 600,000 patients in the U.S., and approximately 1 in 5 of these patients also have atrial fibrillation (AF). The incidence of stroke in HCM patients is markedly increased when complicated by AF. Oral anticoagulants are recommended for stroke prevention, and non-vitamin K antagonist oral anticoagulants (NOACs) may be reasonable alternatives to warfarin. However, little evidence exists regarding the comparative effectiveness and safety of NOACs versus warfarin in AF patients with HCM, making therapeutic decisions difficult for both patients and clinicians. This study aimed to compare the risk of stroke and major bleeding in patients with HCM and AF treated with NOACs or warfarin.
Methods: Using a large U.S. commercial insurance database, we identified privately insured and Medicare Advantage patients with HCM and AF who were users of NOACs or warfarin between 10/1/2010 and 4/30/2015. We created a propensity-matched cohort consisted of 568 NOACs and 859 warfarin users. Cox proportional hazards models were used to assess the time to the first inpatient admission for stroke or systemic embolism (effectiveness outcome) or major bleeding (safety outcome) occurring on therapy.
Results: Over 639 person-years of follow up, the incidence rates for stroke or systemic embolism were similar between NOAC and warfarin-treated patients (1.93 and 2.03 events per 100 person-years for NOAC and warfarin, respectively). The incidence rates for bleeding were not statistically different (4.18 and 5.38 for major bleeding, 0.32 and 1.22 for intracranial bleeding, and 3.22 and 4.06 for gastrointestinal bleeding for NOAC and warfarin, respectively. The hazard ratios (95% confidence intervals) comparing NOACs with warfarin (reference) were: 0.92 (0.32-2.63) for stroke or systemic embolism, 0.75 (0.36-1.57) for major bleeding, 0.26 (0.03-2.25) for intracranial bleeding and 0.77 (0.33-1.82) for gastrointestinal bleeding.
Conclusions: In general practice settings, NOACs use was associated with similar risks of stroke and bleeding compared with warfarin in patients with HCM and AF.

AB35-04

COMPUTATIONAL THREE-DIMENSIONAL LEFT ATRIAL APPENDAGE WALL THICKNESS MAPS AND HISTOLOGICAL ANALYSIS TO GUIDE LEFT ATRIAL APPENDAGE ELECTRICAL ISOLATION

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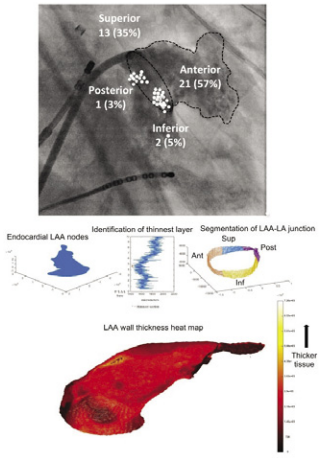
Introduction: Left atrial appendage (LAA) electrical isolation may improve the efficacy of persistent atrial fibrillation (AF) ablation. We have previously demonstrated substantial acute LAA reconnection rates in both canines and humans following electrical isolation. We sought to establish whether LAA ostial thickness variations could be evaluated by a novel computational algorithm applied to a pre-procedure CT.
Methods: LAA wall thickness was calculated by solving the Laplace equation between the boundary conditions assigned to the endo- and epi-cardial surfaces from CT scans of 20 patients Comparison was made with acute LAA reconnection sites in 20 patients with longstanding persistent AF undergoing LAA isolation following conventional AF ablation and with ostial LAA thicknesses from a group of cadaveric human hearts without previous ablation matched with the ablation group.
Results: The anterior (2.5±0.8mm) and superior (2.4±1.2mm) LAA margins were thickest histologically. This correlated with recorded sites of acute reconnection. The algorithm calculated thicker tissue at the same ostial sites. The thickest region was at the anterior wall; the inferior wall was the thinnest (2.4±1.5mm vs 1.8±0.8mm, p = 0.039).
Conclusions: Additional LAA electrical isolation may improve persistent AF ablation efficacy. Acute LAA reconnection rates are substantial, and correlate with regions of thicker ostial tissue. This novel algorithm allows accurate delineation of LAA ostial sites with thickest tissue and correlates with clinically observed reconnection sites and with histological analysis. Identification of these sites may improve ablation efficacy and durability of LAA isolation.



AB35-05

TREATMENT AND RISK FACTORS ASSOCIATED WITH LEFT-ATRIAL THROMBUS FORMATION AFTER PLACEMENT OF THE WATCHMAN OCCLUSION DEVICE

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Introduction: Closure of the left atrial appendage (LAA) is being commonly used in patients with atrial fibrillation (AF) who are poor candidates for long term oral anticoagulation (OAC). Thrombus formation over the device necessitates continuation or restarting of OAC. There are no guidelines to manage this subset of patients. We studied risk factors associated with thrombus formation and assessed the results of the our center's treatment strategy.
Methods: We retrospectively analyzed 149 patients who

underwent Watchman device (WD) implant at our site between 2007 and 2011. All patients had baseline TTE and TEE before placement of a WD. Post-implant TEE was repeated at 45 days, 6 and 12 months. All patients were treated with warfarin for 30 days post-implant. Warfarin was discontinued when no thrombus was seen at follow-up TEE. All patients with thrombus formation were started on a 3-month regimen of warfarin with a target INR of 2.5-3.5. A repeat TEE was performed at 3 monthly intervals to assess for clot resolution. After complete resolution of the thrombus, warfarin was continued for another 3 months to allow for endothelialization. These patients underwent another TEE at 3 months after warfarin discontinuation to assess for recurrence of thrombus formation.

Results: Patients that developed LA thrombus had lower EF, larger LA, higher incidence of LA spontaneous contrast. All patient but one who developed LA thrombus, had thrombus resolution within treatment protocol and successfully discontinued OAC. No thromboembolic events were noted.

Results			
	No Thrombus	LA Thrombus	P Value
Total Patients (149)	142	7	
Mean Age	75	79	0.089
CHF	31%	28%	0.86
HTN	86%	100%	0.29
Stroke/TIA	15%	28%	0.35
Average Ejection Fraction	52%	49.2%	0.54
Average CHADS2 Score	2.1	2.9	0.059

Conclusions: Our treatment strategy was highly successful for management of LA thrombus and eventual discontinuation of OAC after WD implant.

AB35-06

BURDEN OF ATRIAL FIBRILLATION AND THROMBOEMBOLISM RISK: THE RHYTHM STUDY

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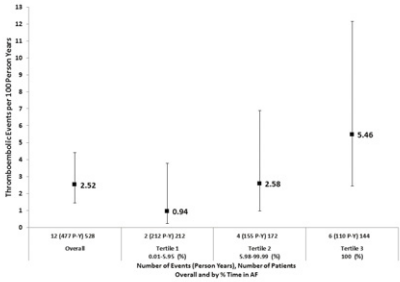
Introduction: Limited evidence exists about whether duration of atrial fibrillation (AF) independently increases the risk of ischemic stroke and systemic thromboembolism.

Methods: We identified all members of Kaiser Permanente Northern and Southern California who underwent 14-day continuous ambulatory ECG monitoring using the ZIO® Patch (iRhythm) between Oct 2011-May 2014 and were found to have AF (minimum episode duration 30 sec). AF duration was calculated as % of total analyzable wear time. Patient characteristics and ATRIA stroke risk score were obtained from electronic medical records. Physician-adjudicated thromboembolic events (TEE) off anticoagulants were based on electronic medical records through Dec 2014.

Results: Overall, 793 adults had AF on ZIO® Patch, with mean age 70 yrs, 40% women, 8% prior stroke/TIA, 19% heart failure, 70% hypertension, 22% diabetes and 28% eGFR <60 ml/min/1.73 m2. During follow-up, there were 12 validated TEE that occurred off anticoagulants (rate 2.52 per 100 person-years), with a higher crude rate with greater % time in AF (Figure). After adjustment for ATRIA stroke risk score, there was a 9% increased odds of TEE per 10% increase in % time in AF (adjusted OR 1.09, 95%CI:0.97-1.23) that was borderline significant.

Conclusions: Increasing burden of AF off anticoagulation may be linearly associated with a higher risk of thromboembolism even after accounting for underlying predicted stroke risk. Cohort expansion and additional follow-up for events is underway. If confirmed, assessment of time in AF could improve personalized anticoagulation decision-making.



ABSTRACT AB36: CRT: The LV Lead: Optimizing Location and Pacing Configuration

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB36-01

WITHDRAWN

AB36-02

INCIDENCE AND PREDICTORS OF PHRENIC NERVE STIMULATION FOLLOWING CARDIAC RESYNCHRONIZATION THERAPY SYSTEM IMPLANTATION OF A QUADRIPOLAR LEAD

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Introduction: Quadripolar (quad) left ventricular (LV) pacing leads are routinely used during cardiac resynchronization therapy (CRT). When phrenic nerve stimulation (PNS) occurs in patients with a quad LV lead, reprogramming is often sufficient to eliminate the problem. However, the incidence and predictors of PNS remain less understood.

Methods: Patients implanted with CRT-D during a prospective Investigational Device Exemption study of the Boston Scientific ACUITY X4 quad LV lead were evaluated. Electrical performance including pacing capture thresholds (PCT) and PNS were evaluated intra-operatively (IO), at pre-discharge, and 3 months. The IO PNS safety margin was calculated between PNS (tested up to 7.5V) and PCT. Complications were tracked for 6 months.

Results: Clinically documented PNS occurred in 58 (8%) of 744 CRT patients. In 14 (24%) of these patients, PNS occurred within the first day of implant; overall, the median time to PNS was 5.5 days [IQR 0.75, 53]. PNS most commonly occurred when the distal electrode was used (30 of 205 [15%] cases vs 28 of 539 [5%] for non-distal pacing, p<0.001). In 51 (88%) of the 58 patients, PNS was not present IO at even maximal pacing output. In the remaining 7 patients, a safety margin between PNS and PCT failed to prevent PNS. When the safety margin

was < 2 V, there was 35% risk of PNS. Device reprogramming (lowering pacing output or changing pacing electrode) was sufficient to eliminate the issue in 55 (95%) cases.
Conclusions: With an ACUITY X4 quad LV lead, PNS was observed in 8% of patients, often within days of device implantation. When possible, avoidance of the distal electrode for pacing and avoidance of accepting a small “safety margin” for pacing output may mitigate against PNS. However, most patients had no measureable PNS at implant, suggesting an inability of current IO techniques to ensure subsequent absence of PNS.

AB36-03

THE USE OF VELOCITY VECTOR IMAGING AND LV CIRCUMFERENTIAL STRAIN ANALYSIS IN MULTIPOINTTM QUADRIPOLAR PACING

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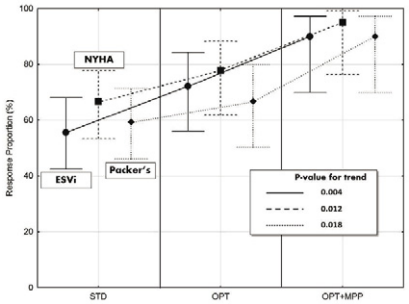
Introduction: MultipointTM Pacing (MPP) using a quadripolar lead may improve cardiac resynchronization therapy (CRT) by creating a more uniform propagation across the left ventricle (LV). Echocardiography with Velocity Vector Imaging (VVI) analysis provides an accurate assessment of acute resynchronization post implant. We report our initial experience using VVI post CRT implant to assess acute resynchronization response to MPP.
Methods: 13 patients (7 males/6 females, 72+5 yrs old, LV EF 25+6%, 8 ischemic/5 non-ischemic pts) with LBBB & Class III CHF underwent CRT implant with a quadripolar LV lead (SJM, Sylmar, CA). LV lead location was posterolateral, lateral, or anterolateral in 12 patients with an anterior location in 1 pt (no other suitable targets). Real time 6 segment LV circumferential tissue strain analysis using VVI software (Siemens, Mountainview, CA) was performed at 3M & 6M post-implant. Pacing vectors were eliminated if the LV thresholds were > 2.5V or if PNS was present. The vectors with the greatest RV-LV delays were then selected for MPP & resynchronization assessment was performed. A 6 segment time-to-peak (TTP) strain of opposing segments <130 ms was defined as dyssynchrony.
Results: MPP vectors resulted in resynchronization in 12/13 (92%) pts. Resynchronization was not achieved with either BiV or MPP vectors in the patient with the anterior LV lead location. MPP vectors had a higher rate of resynchronization compared to BiV vectors (69/125, 55% vs 44/118, 45%, p<0.005, chi square test). Linear stimulation with MPP to a dual anodal RV coil had the highest rate of resynchronization compared to MPP to a single RV coil and MPP to no RV coil (68% vs 57% vs 46% respectively).
Conclusions: MPP resulted in acute resynchronization in over 90% of CRT patients assessed by LV circumferential strain analysis and demonstrated an overall higher resynchronization rate compared to BiV pacing. Linear stimulation with MPP in a dual anodal RV coil configuration resulted in the highest rate of resynchronization.

AB36-04

ACUTE OPTIMIZATION OF LEFT VENTRICULAR PACING SITE PLUS MULTIPOINT PACING IMPROVES REMODELING AND CLINICAL RESPONSE OF CRT AT ONE YEAR FOLLOW UP

Francesco Zanon, MD, FHRS, Enrico Baracca, MD, Gianni Pastore, MD, Lina Marcantoni, MD, Loris Roncon, MD, Franco Noventa, MD and Frits W. Prinzen, PhD. Ospedale S. Maria Della Misericordia, Rovigo, Italy, University of Padua, Padova, Italy, Maastricht University, Maastricht, Netherlands

Introduction: One third of heart failure (HF) pts treated with cardiac resynchronization therapy (CRT) fail to respond. The optimization of the pacing site of the left ventricle (LV) contributes to better CRT response. The MultiPoint (MPP) pacing of the LV has shown preliminary improvements in clinical outcomes. The purpose of our study was to test the hypothesis that pts optimized at implant and treated with MPP experience superior long-term clinical outcomes than conventional CRT pts.
Methods: 110 HF pts treated for 1 year with either conventional CRT (STD, N=54), CRT with hemodynamic and electrical optimization of LV pacing site (OPT, N=36), optimization of LV pacing site + MPP (OPT-MPP, N=20) were evaluated to determine CRT response relative to baseline. Responders were classified in terms of 1-year reduction in end-systolic volume index≥ 15%, reduction in NYHA class≥1, and PACKER score variation (NYHA response with no HF-related hospitalization or death).
Results: In terms of ESVi, 55.6% of STD, 72.2% of OPT, and 90.0% of OPT-MPP pts were responders. In terms of NYHA, 66.7% of STD, 77.8% of OPT, and 95.0% of OPT-MPP pts responded, with more MPP pts experiencing a NYHA downgrade of 2 classes or beyond. Likewise, 59.3.0% of STD, 66.7% of OPT, and 90.0% of OPT-MPP pts exhibited a 1-year PACKER response.
Conclusions: Optimization of LV pacing sites by means of Hemodynamic and electrical delay plus MPP showed an enhanced potential to reverse the progression of HF and improve clinical outcomes, relative to conventional CRT.



AB36-05

LATE LOCAL ACTIVATION PREDICTS RESPONSE TO RESYNCHRONIZATION THERAPY IN SPITE OF PRESENCE OF ELECTROPHYSIOLOGIC MARKERS SUGGESTIVE OF SCAR

Seth J. Rials, MD, PHD, FHRS, Justin B. Weiner, MD, FHRS, Timothy Meyer, PhD, Michael R. Gold, MD, PHD, FHRS and Kenneth A. Ellenbogen, MD, FHRS. Grant Medical Center, OhioHealth, Columbus, OH, Boston Scientific, St. Paul, MN, Medical University of South Carolina, Charleston, SC, Medical College of Virginia, Richmond, VA

Introduction: Higher response rates to resynchronization therapy (CRT) are seen when LV leads are located at sites of long electrical delay, as assessed by the QLV interval. Separately, presence of scar at the LV lead is associated with poor response to CRT. We hypothesize that EP markers suggestive of scar recorded from LV leads of CRT devices affect response to CRT and alter the predictive value of QLV.
Methods: LV electrograms from the QLV substudy of the Smart AV trial were retrospectively examined by a core lab blinded to clinical outcome. Voltage (V), Duration (Dur), fractionation (#TP),

and presence of late potentials (LP) were measured. Results were then compared between responders and nonresponders and stratified by QLV quartile.
Results: QLV was a strong predictor of response as shown previously. However, there was no significant difference in electrogram voltage, duration, fractionation, or presence of late potentials between CRT responders and non responders (see Table). Presence of late potentials (defined as any turning point after the end of the QRS), was closely correlated with QRS quartile but did not provide additional predictive value. (*=p<0.001 vs CRT nonresponder, +=p<0.01 vs QLV 1st Quartile).
Conclusions: QLV predicts response to CRT regardless of electrogram voltage, duration, fractionation, or the presence of late potentials. The presence of prolonged or fractionated electrograms should not dissuade implanting physicians from an otherwise appropriate pacing site.

	CRT Response		QLV Quartile			
Electrogram Parameter	Yes	No	First	Second	Third	Fourth
n	174	158	90	78	86	78
QLV msec Mean (SD)	102 (33)*	87 (36)	52 (19)	84 (7)**	110 (8)**	141 (15)**
V mV Mean (SD)	12(4)	12 (4)	12 (4)	12 (4)	12 (5)	12 (4)
Dur msec Mean (SD)	111(45)	108 (41)	101(33)	110(37)	112(48)	115(53)
#TP Mean (SD)	5 (2)	5 (2)	5 (1)	5 (2)	5 (2)	5 (3)
LP, n (%)	119 (68)*	68 (43)	12 (13)	33 (42)**	68 (80)**	74 (95)**

AB36-06

COMPARATIVE STRATEGIES FOR OPTIMAL LV LEAD PLACEMENT IN CRT

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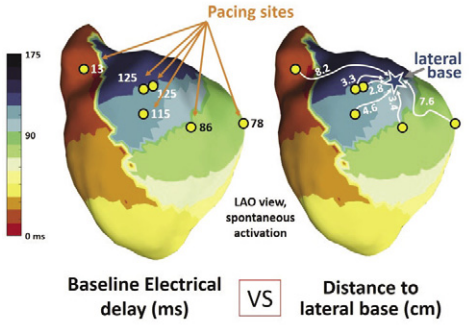
Introduction: This study aimed to compare an anatomical versus a patient specific approach for LV lead positioning. Pacing sites were compared according to their distance from the lateral base (LB) and their electrical delay during spontaneous rhythm.
Methods: Electrocardiographic mapping with invasive LVdP/dtmax measurements were performed during CRT implantation in 34 patients (QRS>120ms). Per procedural tests of different epicardial LV pacing sites were performed in biventricular pacing (BVP) configuration with an apical RV lead. For each patient the pacing sites were divided in groups according to 1) the geodesic distance from the LV base 2) their electrical delay during spontaneous activation. These groups were compared in terms of BVP induced changes in LVdP/dtmax (normalized per patient) and electrical dyssynchrony (ERI: electrical resynchronization index combining total activation time and difference in the mean LV and RV activation time).
Results: The latest activated area was basal in 94% of the patients (43% at the LB). Overall 142 LV (median 4/per pt.) pacing sites were tested. Changes in LVdP/dtmax and ERI were significantly different between the groups according to the distance to LB (the shorter the better; p=0.02 and p<0.01 respectively). ERI but not LVdP/dtmax was significantly different between the groups according to their baseline electrical delay (the later, the better; p=0.01).
Conclusions: Targeting the latest activated area would result in pacing the base in more than 90% of the patients. This strategy is expected to be effective since there is a direct relationship between the distance to the lateral base and both the hemodynamic and electrical response to BVP.



ABSTRACT PLUS AB37: What›s New in CRT?

Friday, May 6, 2016
1:30 PM - 3:00 PM

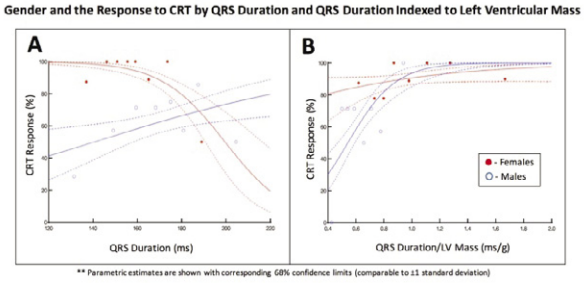
AB37-01

THE PROBABILITY OF RESPONSE TO CARDIAC RESYNCHRONIZATION THERAPY AS A FUNCTION OF QRS DURATION, LEFT VENTRICULAR MASS, AND GENDER IN PATIENTS WITH NON-ISCHEMIC CARDIOMYOPATHY AND LEFT BUNDLE BRANCH BLOCK

Jason Lappe, MD, Nanda Pullela, MD, Mahesh Manne, MD, Jiayan He, ScD, Patrick Tchou, MD and Niraj Varma, MD, PhD. Cleveland Clinic, Cleveland, OH

Introduction: Gender differences in response rates to cardiac resynchronization therapy (CRT) at a given QRS duration (QRSd) are well described. Left ventricular mass (LVM) is affected by QRSd. Therefore, we hypothesized that the relationship between CRT response and QRSd would be improved by indexing for LVM.
Methods: This single center, retrospective study evaluated patients with non-ischemic cardiomyopathy and LBBB undergoing CRT implant between 2000-2007. Echo measurements were obtained prior to the procedure and 3-12 months post. Pre-implant LVM was measured using biplane imaging with measurements of the endocardial and epicardial borders, application of the modified Simpson's rule, and correction for myocardial density. CRT response was defined as improvement in follow-up ejection fraction (EF).
Results: We identified 130 patients (55% female, mean EF 19.1 ± 7.12%, QRSd 165 ± 19.9ms, and LVM 220 ± 83g). CRT response occurred in 65/72 (90%) female vs 36/ 58 (62%) male patients (P<0.01). Baseline QRSd did not differ between responders and non-responders (164 ± 17.6ms vs. 168 ±26.2ms; p=0.22). However, LVM was lower in responders (202 ± 73.4g vs. 282 ± 85.3g, p<0.001). When QRSd was indexed to LVM, the ratio was higher in responders (0.91 ± 0.33ms/g vs. 0.65 ± 0.25ms/g; p<0.001). Gender differences in CRT response rates across QRS durations are shown (Fig A). QRSd indexed to LVM exhibited a strong correlation with CRT response (p=0.0004)(Fig

B). For both men and women, a ratio of QRS duration to LVM of >1.0 resulted in >90% response to CRT.
Conclusions: Gender differences in CRT response may be partially explained by differences in LVM. Indexing QRS duration to LVM may improve prediction of CRT response.



AB37-02

BODY MASS INDEX AND LONG-TERM SURVIVAL IN CARDIAC RESYNCHRONIZATION THERAPY

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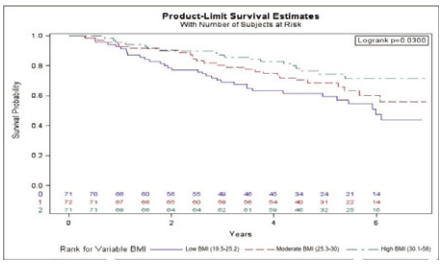
Introduction: The obesity paradox is well known in heart failure, but data is limited for patients receiving cardiac resynchronization therapy with defibrillator (CRT-D). We evaluated the association of body mass index (BMI) with mortality in patients receiving CRT-D.
Methods: Patients that received CRT-D at Montefiore between 1/2005 - 1/2008 were included. Cohort was divided based on BMI: low (N= 71, 19.5-25.2 kg/m2), moderate (N= 72, 25.3-30 kg/m2) and high (N= 71, 30.1-58 kg/m2). Mortality data was ascertained from the Social Security Death Index or hospital records through 1/2012. Continous and categorical data are presented in means and frequencies, respectively. Kaplan-Meier survival analysis and Cox proportional hazards were performed.
Results: There were 214 patients with mean age 66±12, BMI 29±6.7 and pre-implant ejection fraction (EF) of 28±9%. Median follow up was 4.5 years. Among study groups (low, moderate, and high BMI), age was 68±13, 68±9 and 62±11 (p= 0.0007), and non-responders were 42%, 46% and 38%, respectively (p=0.5303). High BMI had the longest survival (54%, 64 and 75%, respectively; p= 0.03, figure 1). When compared to low BMI, high BMI was less likely to have all-cause mortality (HR 0.47, 95%CI 0.26 - 0.83). However, after adjustment for age, baseline EF, and CRT-D response, only age (HR 1.042, 95%CI 1.02 - 1.07) and CRT-D response (HR 0.57, 95% CI 0.353 - 0.922) were significant predictors of survival.
Conclusions: Our study does not show an independent association between BMI and survival. Age and CRT-D response determined the increased survival seen in our population.



AB37-03

CARDIAC VEIN ACCESSIBILITY ACCORDING TO HEART DISEASES AND SEX: IMPLICATIONS FOR CARDIAC RESYNCHRONIZATION THERAPY

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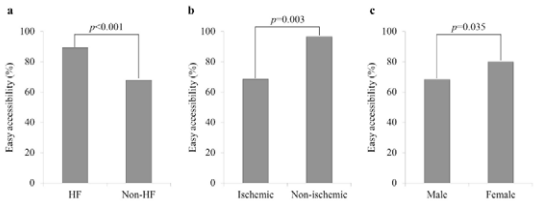
Introduction: Cardiac resynchronization therapy (CRT) is an important therapy in patients with heart failure (HF) and dyssynchrony. We performed the present study to elucidate clinical factors associated with cardiac vein accessibility.
Methods: In consecutive 255 patients (age, 48.7 ± 19.4 years; male, 126), cardiac venography was performed during CRT implantation or an electrophysiological study. We measured the diameters and the proximal branching angles of the lateral cardiac and posterior ventricular veins. Easy accessibility of the cardiac vein was defined as a lumen diameter ≥ 1.6 mm with an angle of ≥ 90°. We compared baseline characteristics between patients with and without easily accessible cardiac veins. We compared cardiac vein accessibility between patients with and without HF, including ischemic and non-ischemic HF, and between males and females.
Results: In 189 (74.1%) patients, the cardiac veins were easily accessible. The cardiac veins were more easily accessible in patients with HF (n = 75) compared with patients without HF (n = 180) (89.3% and 67.8%, respectively; P < 0.001). The cardiac veins were more easily accessible in patients with non-ischemic HF (n = 56) compared with patients with ischemic HF (n = 19) (96.4% and 68.4%, respectively; P = 0.003). The cardiac veins were more easily accessible in females compared with males (79.8% and 68.3%, respectively; P = 0.035).
Conclusions: Accessing the cardiac veins for CRT implantation was difficult in ~10% of patients with HF. Cardiac vein accessibility was high in patients with non-ischemic HF and in females.



AB37-04

'WAVE FRONT FUSION DURING BIVENTRICULAR PACING AND CONSEQUENCES FOR ACUTE HEMODYNAMIC BENEFIT'

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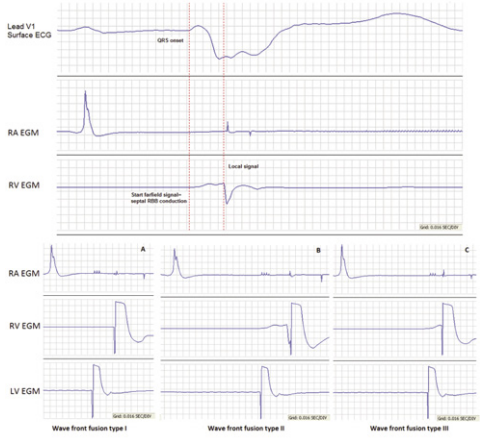
Introduction: Depending on intrinsic atrioventricular (AV) conduction, programmed AV delay, and interventricular (VV) delay 3 types of wave front fusion can occur during biventricular pacing (BiVp) ; I) fusion of right and left ventricular pacing (resp. RVp, LVp) wave fronts, II) fusion of intrinsic right bundle branch (RBB) conduction with LVp wave front, and III) RBB conduction fused with both RVp- and LVp wave fronts. This study aimed to compare acute hemodynamic benefit of BiVp by wave front fusion type.
Methods: In 18 patients with intact AV conduction AV and VV delays were optimized based on LV pressure rise (LV dP/dtmax) during CRT device implantation. Combinations of 4 AV delays (20, 40, 60 and 80% of intrinsic right atrial to RV conduction time) with respectively 7 VV delays (-80 to 20ms) were tested. Per combination, wave front fusion type was assessed on intra-cardiac electro grams (EGM). Fusion with RBB conduction during BiVp was noted on RV EGM as far field signal prior to RVp (fig. 1). Maximal LV dPdtmax change by wave front fusion type was assessed and compared.
Results: Optimization matrix allowed all wave front fusion types to occur in every patient. Maximal LV dPdtmax increase was reached with wave front fusion type I in 56% of patients, in 44% with type III and in none with type II. Median maximal LV dPdtmax increase was 21.9%(7.8%) for type I, 22.1%(5.8%) for type III and 15.6%(2.9%) for type II (P<0.001).
Conclusions: Wave front fusion of LVp with RVp (type I) or with RVp and RBB conduction (type III) during BiVp is associated with significantly more acute hemodynamic benefit in comparison to BiVp without contribution of RVp (type II).



AB37-05

CHANGES IN ELECTRICAL HETEROGENEITY OF BODY SURFACE MAPS: APPLICATION FOR CRT OPTIMIZATION

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Introduction: Reduction of electrical heterogeneity with CRT may be an important mechanism of response. Changes in paced QRS duration have not been very useful for optimization. Better methods of quantifying electrical heterogeneity using body surface isochrone mapping may help to personalize CRT to minimize heterogeneity and maximize response.
Methods: A 55-electrode body surface mapping system with anterior and posterior arrays was used to calculate the standard deviation of activation times (SDAT) in 84 subjects. Lower SDAT implies reduced heterogeneity and better resynchronization. SDAT was measured at baseline CRT, native rhythm (or RV paced if needed), different atrioventricular and interventricular delays, and LV only pacing. Optimization potential was defined as % change in SDAT from programmed to optimal setting.
Results: SDAT decreased 19 ± 27% from native to programmed CRT (41 ± 12 to 32 ± 11 ms, p<0.01). Optimal SDAT was 22 ± 8 ms and was 27 ± 22% lower (p<0.01) than programmed. Subjects with LBBB tended to have greater native SDAT (41 ± 10 vs. 36 ± 14ms, p=0.09), but no difference in optimization potential (28 ± 24 vs. 25 ± 16%, p=0.55). Patients with QRS ≥ 150 had greater native SDAT (43 ± 12 vs. 35 ± 12ms, p<0.01), but no difference in SDAT improvement at baseline (21 ± 28% vs. 14 ± 26%, p=0.34) or optimal CRT (28 ± 23 vs. 24 ± 18%, p=0.43). Optimal pacing mode was: BiV 26%, LV only 24%, either BiV or LV only 44%, native 5%, and RV only 1%. Optimal SDAT required LV pre-excitation by 10-60 ms in 61% of patients.
Conclusions: CRT at baseline programming improves electrical heterogeneity by 19% with the potential for a further 27% improvement with optimization. Optimization potential is similar in patients with or without LBBB and with QRS ≥ 150 or 120-149ms. Optimal setting was achieved in 68% of patients with LV only pacing and in 61% with LV pre-excitation when BiV paced. Body surface mapping offers the possibility of assessing electrical heterogeneity at multiple device settings and improving CRT response by individualizing device programming to minimize heterogeneity.

ABSTRACT AB38:
New Prognostic Data in Heart Failure

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB38-01

CONTEMPORARY TREATMENT OF ATRIAL FIBRILLATION IN HEART FAILURE WITH REDUCED EJECTION FRACTION AMONG US CARDIOLOGY PRACTICES AND THE POTENTIAL FOR UPTAKE OF CATHETER ABLATION: AN NCDR RAPID REGISTRY RESPONSE PROJECT

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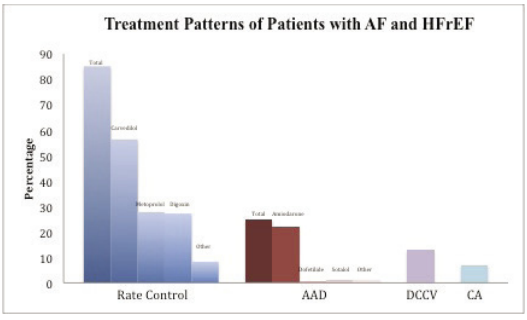
Introduction: Atrial fibrillation (AF) and heart failure with reduced left ventricular ejection fraction (HFrEF) frequently coexist. The recent Ablation versus Amiodarone for Treatment of persistent Atrial fibrillation (AF) in patients with Congestive heart failure and an implantable device (AATAC) trial suggests that

catheter ablation can provide benefit to these patients, but how these findings apply to current treatment patterns in the AF and HFrEF population are unclear.
Methods: Using the outpatient NCDR PINNACLE Registry, we identified participants with AF and HFrEF seen between 1/2013-12/2014. Treatment with AV-nodal blocking agents, anti-arrhythmic drugs (AAD), or a history of catheter ablation (CA) was assessed at time of inclusion into the registry.
Results: We evaluated 36,786 patients with AF and HFrEF treated at 878 cardiology sites. Mean age was 73.2±11.5 years and 72.9% were male. Comorbidities included coronary artery disease (75.3%), hypertension (83.3%), and diabetes (32.0%). AF was predominantly paroxysmal (67.2%) rather than persistent/permanent (17.4%) or new onset (15.4%). AV-nodal blocking agents were used in 85.0% with carvedilol (56.3%), metoprolol (27.8%), and digoxin (27.2%) seen the most frequently. A rhythm control strategy with AAD was reported in 25.0% of patients; 21.8% of the total population were using amiodarone. Of the cohort, 13.0% had a history of cardioversion and 6.8% had previously undergone CA.
Conclusions: AF treatment in patients with HFrEF predominantly consisted of rate control, and few had a history of CA. Translation of the AATAC findings to current clinical practice may result in an increase in CA among this population.



AB38-02

IMPACT OF ATRIAL FIBRILLATION ON PUMP THROMBOSIS AND THROMBOEMBOLIC EVENTS IN LONG-TERM LEFT VENTRICULAR ASSIST DEVICE THERAPY

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Introduction: Pump thrombosis (PT) and thromboembolic events (TEE) are severe complications in long-term left ventricular assist device (LVAD) therapy. The aim of the present study is the evaluation of impact of atrial fibrillation on these events in patients supported with HeartWare HVAD (HW).
Methods: Incidence of visually confirmed PT and TEE such as peripheral arterial embolism and cerebral embolism was retrospectively analyzed in patients supported with primarily implanted HW (n=250) that were implanted between 10/2012 and 06/2015 at our institute. Patients were divided into those suffering from atrial fibrillation (AF n=185) and those showing sinus rhythm (SR n=65) before surgery.
Results: Median support time for all patients was 1.33 years (0-2.95) and 354 patient years. Patients with AF showed 0.05 events per patient year (EPPY) for PT vs. 0.08 EPPY in the SR group (p=0.441). Patients with AF showed 0.1 EPPY for TEE vs 0.05 EPPY in the SR group (p=0.120). Kaplan-Meier analysis of survival probability showed no difference between the two groups.
Conclusions: Our preliminary study showed that preoperative AF has no impact on PT and TEE. We are currently evaluating 400 more patients to increase the power of our analysis and will present the results at the congress.

AB38-03

PREDICTORS OF STROKE IN HEART FAILURE PATIENTS WITHOUT ATRIAL FIBRILLATION

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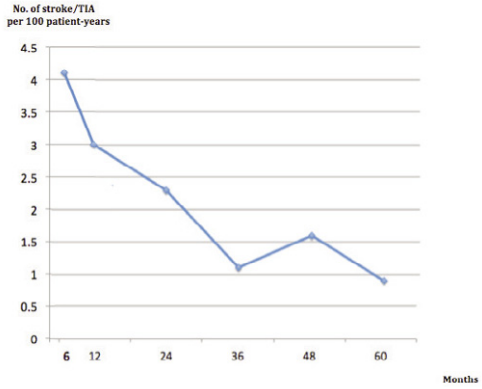
Introduction: Heart Failure (HF) patients have an increased risk of ischemic stroke / transient ischemic attack (TIA). While anticoagulation is recommended for those with atrial fibrillation (AF), treatment for those without AF remains uncertain. This study sought to identify the risk factors for stroke / TIA among HF patients without AF who may benefit from anticoagulation therapy.
Methods: We conducted a retrospective, observational study on consecutive patients hospitalized for new-onset HF between 2005 and 2012 in our institution. Predictors for ischemic stroke / TIA among those without AF were studied in a multivariate Cox regression model.
Results: A total of 1,940 patients were hospitalized for new-onset HF, of which 1,234 had no AF at baseline (mean age 77.3±12.4 years, 51.7% female). After a mean follow-up of 39.5±31.1 months, 116 (9.4%) of those without AF developed ischemic stroke / TIA (Figure). Univariate analysis revealed that age [HR 1.32 per decade (1.11-1.57), p=0.002], hypertension [HR 1.79 (1.13-2.85), p=0.01], vascular disease [HR 1.18 (1.02-3.23), p=0.04] and severe chronic kidney disease [HR 1.43 (1.18-1.74) from stage III to stage V, p<0.001] predicted stroke / TIA in HF patients without AF. In the multivariate model, age [HR 1.54 (1.25-1.89) per decade, p<0.001] and severe chronic kidney disease [HR 1.38 (1.11-1.72) from stage III to stage V, p=0.004] remained independently predictive of stroke / TIA in HF patients without AF.
Conclusions: Our results showed that HF without AF is associated with a high incidence of ischemic stroke / TIA. Old age and severe chronic kidney disease independently predicted a high-risk subset who may benefit from anticoagulation therapy.



AB38-04

THE CHARACTERISTICS OF LEFT VENTRICULAR LATE GADOLINIUM ENHANCEMENT PREDICT CLINICALLY SIGNIFICANT ARRHYTHMIC EVENTS IN PATIENTS WITH NONISCHEMIC CARDIOMYOPATHY

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Introduction: Left ventricular late gadolinium enhancement (LV-LGE) in cardiac magnetic resonance (CMR) is known to be related to adverse clinical outcomes in patients with nonischemic cardiomyopathy (NICM). However, an association between the characteristics of LGE and arrhythmic risk has not been demonstrated with consistency in NICM.
Methods: Three hundred sixty-five consecutive patients (54±15years) with angiographically proven NIDC who underwent cardiac MR were enrolled for this study. All patients were followed up for the major ventricular arrhythmias (VA) including sustained ventricular tachycardia (VT), appropriate implantable cardioverter-defibrillator (ICD) intervention and ventricular fibrillation (VF).
Results: LV-LGE was identified in 267 (73 %) patients. During 44.3 ± 36.4 months of follow up, patients with LV-LGE had higher incidence of total VA (14% vs. 6%, p=0.03). In multivariate analysis, independent predictors of total VA were the presence of LV-LGE (HR 2.78; 95% CI 1.10-7.02; p=0.03), extensive LV-LGE (adjusted HR 3.75, 95% CI 1.76-7.80, p=0.001) and subepicardial LV-LGE (adjusted HR 4.75, 95% CI 1.73-13.04, p=0.003). Moreover, extensive LV-LGE (adjusted HR 3.44, 95% CI 1.00-11.86, p=0.049) and subepicardial LV-LGE (adjusted HR 5.67, 95% CI 1.47-21.91, p=0.01) were also independent predictors of major VA. However, location of LV-LGE did not act as a predictor of total or major VA.
Conclusions: In patients with NICM, the extensive or subepicardial LV-LGE were independent predictors of total and major VA, suggesting that the extent and patterns of LV-LGE were closely related with the severity of arrhythmic events.

AB38-05

ECCENTRIC HYPERTROPHY PREDICTS SUDDEN CARDIAC DEATH IN SUBJECTS WITH REDUCED LEFT VENTRICULAR FUNCTION

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Introduction: Severely reduced LV systolic function is an established risk factor for sudden cardiac death (SCD), and is used to identify candidates for prophylactic ICD therapy. However, only a minority of these patients will receive an appropriate device therapy during follow-up. We evaluated whether LV geometry provides additional information on SCD risk in subjects with reduced LV ejection fraction (LVEF).
Methods: SCD cases (aged ≥ 18 yrs) occurring over a 13-year period in a Northwestern US metro region were compared with geographic controls. Demographic and clinical data were obtained from lifetime medical records. Archived echocardiograms performed closest and prior to the SCD event were reviewed for LVEF, LV mass index (LVMI), and relative wall thickness (RWT, ratio of wall thickness to cavity diameter). LV geometry was defined as: normal (normal LVMI and RWT), concentric remodeling (normal LVMI, increased RWT), concentric hypertrophy (increased LVMI and RWT), and eccentric hypertrophy (increased LVMI, normal RWT). Analysis was restricted to those with LVEF ≤ 40%.
Results: A total of 246 subjects were included in the analysis. SCD cases (n=172, 68.4±13.4yrs, 79% male) compared to controls (n=74, 66.4±11.9yrs, 72% male) were more likely to have hypertension (79.7% vs 63.5%, p=0.008); while they were similar with respect to diabetes (48.3% vs 43.2%, p=0.470) and obesity (37.8% vs 41.9%, p=0.843). LVEF was lower in cases than in controls (29.3%±7.6 vs 31.8%±6.8, p=0.02). Compared to controls, fewer cases presented with normal LV geometry (35.5% vs 51.4%, p=0.02) and more with eccentric hypertrophy (45.9% vs 25.7%, p=0.004), but there were no significant differences in prevalence of concentric remodeling or concentric hypertrophy. In a multivariate model adjusted for age, sex and LVEF, eccentric hypertrophy remained an independent predictor of SCD (OR 2.3, 95% CI 1.2-4.4, p=0.014).
Conclusions: Eccentric LV hypertrophy was independently associated with SCD in subjects with EF ≤ 40%. LV geometry may prove useful for enhanced SCD risk stratification in subjects with reduced LV function, and warrants prospective evaluation.

ABSTRACT AB39:
Arrhythmias in Congenital Heart Disease

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB39-01

LEAD EXTRACTION IN ADULTS WITH CONGENITAL HEART DISEASE

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Introduction: Indications for device implantation are increasing in the growing and aging population with congenital heart diseases (CHD). In parallel, the need to extract transvenous leads is rising. However, safety and feasibility data are limited in this challenging population. Herein, we report the results of lead extraction procedures in adults with CHD over a 20-year period.
Methods: N/A.
Results: A prospective registry for lead extraction procedures was initiated at our center in 1995. A total of 110 leads (42% atrial, 58% ventricular) were extracted in 41 adults with CHD, age 41±14, 41% female, during 62 lead extraction procedures. A total of 28 had complex CHD, including 18 with complete transpositions of the great arteries (d-TGA) and a Mustard or Senning baffle. Main indications for extraction were infection in 31 (50%), lead failure in 19 (31%), device upgrade in 7 (11%) and symptomatic thrombosis in 4 (6%) patients. The median time from lead implantation to extraction was 257 [107; 421] months. A laser was required for 52 (47%) leads and a lasso by

a femoral approach in 4 (4%) leads. Complete lead extraction was achieved for 101 leads (92%). Extraction was unsuccessful for 9 ventricular leads (2 failures with locking stylet, 6 with laser, and 1 with lasso). No death in the peri-operative period and no pericardial effusion were observed. However, 1 patient had a pneumothorax and 6 had pocket hematomas. The degree of sub-pulmonary AV valve regurgitation increased in 8 patients (6 with ICD lead). Two patients with d-TGA and Mustard baffles and 1 with l-TGA had severe AV valve regurgitation of the subpulmonary ventricle requiring later surgical repair. After a median of 67 [27-130] months of follow-up after a first extraction procedure, 15 patients underwent additional lead extraction procedures (1 to 3). Three deaths occurred during follow-up, due to septic shock after CardioWest implantation, to heart failure, and to cerebral hemorrhage.
Conclusions: Despite complex anatomical issues, lead extraction can be achieved successfully in most adults with CHD, using advanced extraction techniques. Subpulmonary AV valve regurgitation is a prevalent (7%) complication, which occasionally requires surgical repair, particularly in patients with TGA.

AB39-02

TRANSCATHETER PULMONARY VALVE IMPLANT ALTERS ELECTROPHYSIOLOGIC SUBSTRATE

Hoang Nguyen, MD, Shabana Shahanavaz, MBBS, George F. Van Hare, MD, FHRS, Balzer T. David, MD, Joshua J. Murphy, MD, Ramzi T. Nicolas, MD and Jennifer N.A. Silva, MD. Washington University in St. Louis, St. Louis, MO, Washington University, Saint Louis, MO, Washington University St. Louis, St. Louis, MO

Introduction: Trans-catheter pulmonary valve implant (Melody Valve, Medtronic, Inc.) has become first-line therapy for congenital heart disease patients with right ventricular outflow conduit dysfunction. The aims of this study are to delineate the short and medium-term EP substrate changes and to elucidate the type and prevalence post-Melody valve arrhythmias.
Methods: Retrospective chart review was performed on patients undergoing Melody valve implantations from May 2010 to April 2015.
Results: A total of 106 patients underwent Melody valve implantations, most commonly patients with Tetralogy of Fallot (n=59, 56%) for pulmonary insufficiency (n=52, 49%). Pre-implant, 25 patients (24%) had documented arrhythmias: non-sustained VT (n=9, 8%), frequent PVCs (n=6, 6%), atrial fibrillation/flutter (n=9, 8%), and SVT (n=2, 2%). Post-implant, arrhythmias resolved in 5 patients who previously had non-sustained VT (56%), and 4 patients who had PVCs (67%). New arrhythmias were seen in 13 patients (12%) with 7 (53%) having PVCs and 6 (47%) having non-sustained VT. There was complete resolution by 6 months in 5/7 patients with PVCs and 6/6 with non-sustained VT. Pre versus post-implant ECG parameters were as follows: no difference in HR (78 vs. 79 bpm, p=0.9), or QRSd (139 vs. 134 ms, p=0.4). The mean QTc lengthened immediately post-implant (462 vs. 479 ms, $p < 0.01$). Immediately post- implant, 16 patients (15%) had persistent ST/T changes, 16 (15%) had new/worsening ST/T changes, 7 (7%) had improved ST/T changes, and 2 (2%) had new left anterior fascicular block. At 6 months, there was improvement of ECG findings in 4/16 (25%) persistent ST/T changes and 8/16 (50%) worsening ST/T changes. Two (2%) patients had worsening ST/T changes.
Conclusions: Melody valve implantation in congenital heart disease patients did reduce the prevalence of non-sustained VT. The majority of post-implant arrhythmias resolve by 6 months follow up. Over 50% of ECG ST/T abnormalities improved post-implant.

AB39-03

ATRIOVENTRICULAR NODAL REENTRANT TACHYCARDIA IN PATIENTS WITH CONGENITAL HEART DISEASE: OUTCOME AFTER CATHETER ABLATION

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Introduction: The relationship of AV nodal reentrant tachycardia AVNRT) to congenital heart disease (CHD) and the outcome of catheter ablation in this population have not been studied in detail.
Methods: A multicenter retrospective study was performed to collect data on patients with CHD who had AVNRT diagnosed during an EP study and treated with radiofrequency or cryothermal ablation.
Results: There were 109 patients (61 females), age at EP study 22.1±13.4 yrs, BSA: 1.61±0.36 m2. The majority (94/109, 86%) had CHD resulting in right heart pressure and/or volume overload. Acute success of catheter ablation was achieved in 90%, with long term success after repeat procedures in 94%. Chronic pacing was required in 5.5%. Patients were divided in two groups based on complexity of CHD: Group A (n=51) with complex CHD, including Ebstein's anomaly, partial or complete AV canal, tetralogy of Fallot, transposition complexes, single ventricle and other; and group B(n=58) with simple CHD including atrial and ventricular septal defects, semilunar or mitral valve abnormalities and other. The onset of AVNRT was noticed before any procedure in 33% of group A and 53% in group B patients (P=0.035). Typical AVNRT (slow-fast variety) was less common in group A vs group B (73% vs 91%, P=0.01). There were no statistically significant differences in patients' age, BSA, use of 3D imaging and type of ablation (radiofrequency vs cryoablation). Procedure times were significantly longer in group A vs group B (251±117 vs 174±94 min, P=0.0006) and fluoroscopy times were longer in group A (median 20.8 vs 16.6 min, P=0.037). There were statistically significant differences between the two groups in the acute success of ablation (82.4% vs 96.5%, P=0.04), risk of any degree of AV block (13.7 vs 0%, P=0.004) and need for chronic pacing (12.5% vs 0%, P=0.008). After 3.2±2.7 years of follow-up, long term success was 86.3% in group A and 100% in group B (P=0.004).
Conclusions: AVNRTcan complicate the course of patients with CHD, especially in patients with right heart pressure or volume overload. The outcome of catheter ablation is favorable

in patients with simple CHD. Patients with complex CHD have increased risk of procedural failure and AV block.

AB39-04

INFLUENCE OF SHUNT TYPE ON VENTRICULAR ARRHYTHMIAS AFTER NORWOOD PROCEDURE

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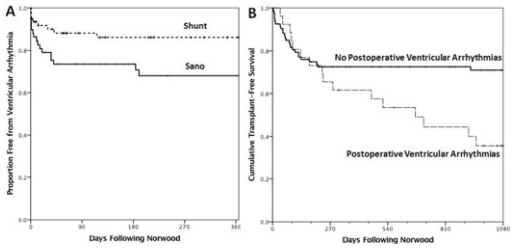
Introduction: Transplant-free survival for single right ventricle (RV) lesions remains <70% at 3 years. Arrhythmia burden, associated influence of shunt type at Norwood procedure (Sano vs Blalock-Taussig shunt [BTS]), and implications for mortality risk are not well defined.
Methods: Single center retrospective analysis of patients with single RV lesions enrolled September 2007-2015 in an ongoing prospective study of arrhythmias after congenital heart surgery.
Results: Of 120 patients, 58 received Sano and 62 BTS at the time of surgery, with median post-Norwood follow-up of 773 days. Amongst all types of arrhythmias, only ventricular arrhythmias (VAs) differed between groups, which were more common in pts receiving Sano (29% Sano vs. 14% BTS, P .049). VAs included 15 with monomorphic VT, 1 polymorphic VT, 3 accelerated ventricular rhythm (AVR) prompting intervention, and 7 AVR untreated. Sano was independently associated with more VAs in multivariate logistic regression (OR 2.6, P .048), and lower freedom from VA during follow-up by Cox regression (HR 2.3, P .045) (A) after accounting for other differences in the BTS and Sano cohorts. Although VA did not impact survival among all pts, among interstage survivors to Glenn palliation (n=86), a history of VA conferred >13-fold increased risk of death (HR 13.5, P<.001) (B).
Conclusions: In this cohort, patients with single RV lesions receiving Sano at the time of Norwood surgery had an increased incidence of ventricular arrhythmias as compared to patients with BTS. Ventricular arrhythmias may impact late mortality in patients who survive the interstage period.



AB39-05

SLOW CONDUCTING ELECTROANATOMICAL ISTHMUSES: THE MISSING LINK BETWEEN QRS DURATION AND VENTRICULAR TACHYCARDIA IN PATIENTS WITH REPAIRED TETRALOGY OF FALLOT

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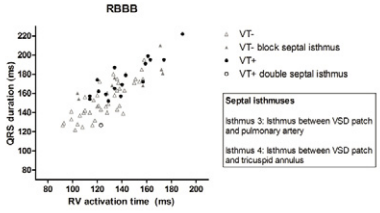
Introduction: Slow conducting anatomical isthmuses (SCAI) with conduction velocity (CV) during sinus rhythm <0.5m/s are related to >90% of induced VTs in repaired TOF (rTOF). Localized conduction delay in infundibular SCAI (isthmus 3 and 4) may also further prolong QRS duration in patients (pts) with a preexisting RBBB.
Methods: Sixty-seven rTOF pts with RBBB underwent programmed stimulation and RV electroanatomical voltage and activation mapping during SR. QRSd, total RV surface area, total RV activation time (RVAT) and CV at anatomical isthmuses (AI) and remote RV sites were measured and compared between pts with and without VT.
Results: Eighteen of 67 pts (36±15 years, 44 male) were inducible for VT, CL 248ms (229 - 304). QRSd and RVAT were significantly longer in pts with VT (173±22 vs 156±20ms, p<0.01 and 141±22 vs 129±21ms, p=0.04). Sixteen of 18 pts with VT had a SCAI, but only 2/49 without VT. Minimal CV through AI was significantly slower in pts with VT (0.4±0.4 vs 0.8±0.2m/s, p<0.01) but remote RV CV and total RV size did not differ between groups (1.1±0.1 vs 1.2±0.2m/s, p=0.31, 241±79 vs 254±64cm², p=0.49). In 17/18 pts with VT, QRSd was >150ms compared to 27/49 pts (55%) without VT (RR 14 (95% CI, 2 - 112), p=0.01). The only patient with VT and QRS≤150ms had SCAI 3 but normal CV of isthmus 4 resulting in normal septal activation. Eight of the 27 pts without VT and QRS>150ms had septal isthmus block excluding reentry but prolonging QRSd.
Conclusions: rTOF pts with VT have localized RV conduction delay confined to anatomical isthmuses. In rTOF pts with preexisting RBBB additional QRS prolongation (>150ms) may be due to SCAI, which may provide an important link between prolonged QRSd and VT.



AB39-06

PREVALENCE AND RISK FACTORS ASSOCIATED WITH LIFE-THREATENING ARRHYTHMIAS IN PATIENTS WITH EISENMENGER SYNDROME

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Introduction: Sudden cardiac death is a major mode of death in patients with Eisenmenger syndrome (ES). Limited data are available on the arrhythmia burden and the risk factors leading up to arrhythmic life-threatening events (LTA) in this population.
Methods: Retrospective review was performed for patients with ES at Boston Children's Hospital (n=93). LTA were defined as sudden cardiac death, need for DCCV, sustained VT, or unexplained syncope.
Results: Mean age at review was 43±17y; 68% were females; and 37% had died at the time of review. Twenty-eight (30%) had Down syndrome. Most common structural anomaly was VSD (32%), followed by AV canal defect (17%). Twenty-six (28%) patients had history of arrhythmia (19% atrial, 12% ventricular). Risk factors for LTA were assessed in those who had a clinical evaluation within 5 years of the event (n=67). In this cohort, lower baseline oxygen saturation (75±9 % vs. 84±8 %, p=0.01) and longer QRS duration (208 ±25 ms vs. 156±66 ms, p=0.004) were associated with LTA; and there was a trend towards association for a higher baseline heart rate (90±13 bpm vs.

79±13 bpm , p=0.07), and female sex (21% in females vs. 4% in males, p=0.08). All patients with LTA had a QRS duration >170 ms and an oxygen saturation <85% (Figure). Severity of echo-determined ventricular dysfunction, shunt location, peak TR jet velocity, use of advanced pulmonary hypertension therapy, anti-platelet therapy or anticoagulation were not associated with LTA.
Conclusions: Patients with ES have a high arrhythmia burden. Wider QRS and lower baseline oxygen saturations are associated with life-threatening arrhythmic events and may be useful in risk stratification of this population.

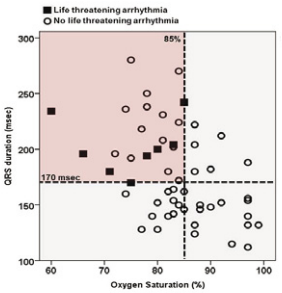

Figure : Scatter plot showing QRS duration and Oxygen saturation in those with (squares) and without (circles) life threatening arrhythmias. All events occurred in those with QRS >170 msec and saturation <85% (pink rectangle).

ABSTRACT AB40: Genetics and Arrhythmias in Children

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB40-01

GENOTYPE PHENOTYPE CORRELATIONS IN PEDIATRIC SCN5A MUTATION CARRIERS

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Introduction: Genotype-phenotype correlations of SCN5A mutations remain unclear. Given the relative rarity of cardiac sodium channelopathies in the pediatric population, risk stratification in the young diagnosed with a given SCN5A mutation need to be clarified.
Methods: A multicenter, international, 1990-2015 retrospective cohort study was conducted in 25 tertiary hospitals in 13 different countries. All patients <16 years of age diagnosed with a genetically confirmed SCN5A mutation, whatever the clinical diagnosis were included in the analysis.
Results: 423 children fulfilled the study inclusion criteria, with a median age of 7.6 (0-16.7) years at diagnosis; 34.7% individuals were probands. Phenotypic spectrum was divided in 76 (18%) isolated LQT3, 33 (7.8%) isolated BrS type 1, 86 (20.3%) isolated PCCD, 3 (0.7%) isolated SSS and 102 (24.1%) overlap phenotypes; 123 (29.1%) kept a negative phenotype throughout follow-up. The risk of arrhythmic event in children was high, especially when a spontaneous LQTS, BrS, PCCD or overlap phenotype was displayed, but also in those with a negative phenotype. Phenotype varied according to mutation type, missense pathogenic mutations being more frequent than radical mutations or variants of unknown significance in isolated LQT3, isolated PCCD and negative phenotype patients. Cardiac arrest or syncope as first symptom, as well as appropriate ICD shocks in implanted patients were more frequently observed in case of mutation located to the transmembrane region. Compound genotype, double SCN5A mutation, sinus node dysfunction, age <1 year at diagnosis and absence of family history of BrS, LQTS, PCCD, PM implantation and cardiac arrest or ICD implantation were independent predictors of cardiac event giving new insights to identify high-risk subgroups in SCN5A mutation positive infants and children.
Conclusions: In the largest series of SCN5A mutation carriers children, we found a high rate of cardiac events; ECG phenotype varied according to mutation type, whereas clinical severity was related to mutation location; several factors emerged as predictors of cardiac arrest or arrhythmic event.

AB40-02

INCIDENTALLY IDENTIFIED VARIANTS IN GENES ASSOCIATED WITH CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA IN A LARGE COHORT OF REFERRALS FOR CLINICAL WHOLE EXOME GENETIC TESTING

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Introduction: The rapid expansion of genetic testing has led to increased utilization of clinical whole exome sequencing (WES). Clinicians are being faced with assessing risk of disease vulnerability from incidentally identified genetic variants, a problem typified by variants found in genes associated with sudden death-predisposing diseases, such as catecholaminergic polymorphic ventricular tachycardia (CPVT).
Methods: Genetic variants from one of the world's largest collections of clinical WES referral tests (Baylor Miraca Genetics Laboratories) were comprehensively reviewed. Variants in CPVT-associated genes, RYR2 and CASQ2, were identified. Healthy control variants with a minor allele frequency <0.01 were obtained from publically-held databases of ostensibly healthy individuals (ExAC). A compendium of putative CPVT-associated variants was compiled from the literature.
Results: Clinical WES reports from 6517 individuals were

compiled which were predominantly pediatric (mean age 9.4 +/- 11.2 years). 580 individuals (8.9%) hosted a variant in CPVT-associated RYR2 and CASQ2 designated as “pathologic” or a “variant of undetermined significance” (VUS). While a small number were classified as “pathologic” (1.2% or 0.1% total cases), 98.8% were designated as VUSs. This was similar to the prevalence of rare variants in RYR2 and CASQ2 among ~60,000 ostensibly healthy individuals (6.7%). Conversely, in the literature, the prevalence of RYR2 mutations in individuals with a diagnosis CPVT, or likely, CPVT was ~47%. Topological mapping of all WES VUSs demonstrated a distribution similar to rare variants from ostensibly healthy individuals and was distinct from disease-associated mutations.
Conclusions: The prevalence of incidental CPVT-associated variants is ~9% in subjects undergoing clinical WES and is similar to the healthy “background” rate of rare variants. CPVT-associated VUSs on WES genetic testing, without prior clinical suspicion for CPVT, are unlikely to represent markers of disease pathogenicity.

AB40-03

RISK FACTORS IN YOUNG PATIENTS WITH BRUGADA SYNDROME

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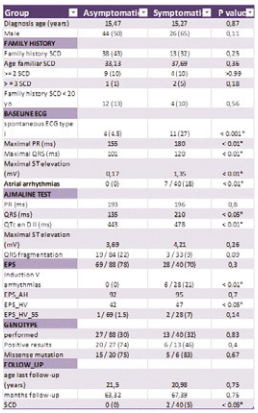
Introduction: BS is a inheritable disease characterised by ST elevation in the right precordial leads and increased risk of SCD. Data on risk in the young population is limited.
Methods: From 1992 to 2015, 1439 individuals underwent an Ajmaline test in our centre: 560 patients were positive, 128 were <= 25 yo. Of these, 88 (69%) were asymptomatic and 40 (31%) had clinical manifestations: 8 (20%) SCD, 30 (75%) severe syncope and 2 (5%) bradycardia/tachycardia syndrome. We compared the 2 groups to identify markers of risk of SCD for BS in the young.
Results: Outcomes are displayed in Image I. No patient from the asymptomatic group died or presented arrhythmia during follow-up. In the symptomatic group, 2 siblings died suddenly: 1 without an ICD (2yo) and the second (18yo) despite his ICD, in a VF storm. 35 symptomatic patients (88%) had an ICD (mean age at implantation 16 +/- 6 years). Of these, 8 (23%) received appropriate shocks. Risk factors for SCD included: Baseline ECG evidence of: 1- spontaneous type I ECG in follow-up; 2- J-point elevation in the lateral or inferior leads > 1mV; 3- sinus node dysfunction; 4- first degree AV bloc with PR > 170ms; 5- QRS length > 120ms; 6- atrial arrhythmias. During Pharmacological test and EPS: 6- abnormal baseline HV interval > 40ms; 7- QRS prolongation > 200ms after Ajmaline infusion (max dose 1mg/kg in 5 min); 8- Induction of ventricular arrhythmias.
Conclusions: Symptomatic BS in the young age is a rare but malignant entity that can manifest early during life with abnormal electrical activity at different levels (sinus dysfunction, atrial tachycardias, AV block, infranodal conduction delay) that may preclude SCD.



Group	Asymptomati	Symptomati	P value
Diagnosis age (years)	15,47	15,27	0,87
Male	44 (50)	26 (65)	0,11
FAMILY HISTORY			
Family history SCD	38 (43)	13 (32)	0,25
Age familiar SCD	32,13	37,69	0,36
>= 2 SCD	9 (10)	4 (10)	>0,99
>= 3 SCD	1 (1)	2 (5)	0,18
Family history SCD < 20 y.o.	12 (13)	4 (10)	0,56
BASELINE ECG			
spontaneous ECG type I	4 (4,6)	11 (27)	< 0.001*
Maximal PR (ms)	155	180	< 0.01*
Maximal QRS (ms)	101	120	< 0.01*
Maximal ST elevation (mV)	0,17	1,35	< 0.01*
Atrial arrhythmias	0 (0)	7 / 40 (18)	< 0.01*
AJMALINE TEST			
PR (ms)	193	196	0,8
QRS (ms)	135	210	< 0.05*
QTc en D II (ms)	445	478	< 0.01*
Maximal ST elevation (mV)	3,69	4,21	0,26
QRS fragmentation	19 / 84 (22)	3 / 33 (9)	0,09
EPS	69 / 88 (78)	28 / 40 (70)	0,3
Induction V arrhythmias	0 (0)	6 / 28 (21)	< 0.01*
EPS_AH	92	95	0,7
EPS_HV	42	47	< 0.05*
EPS_HV_55	1 / 69 (1,5)	2 / 28 (7)	0,14
GENOTYPE			
performed	27 / 88 (30)	13 / 40 (33)	0,83
Positive results	20 / 27 (74)	6 / 13 (46)	0,4
Missense mutation	15 / 20 (75)	5 / 6 (83)	0,67
FOLLOW_UP			
age last follow-up (years)	21,5	20,98	0,75
months follow-up	68,32	67,89	0,76
SCD	0 (0)	2 / 40 (5)	< 0.05*

AB40-04

REFINING GENETIC TEST INTERPRETATION FOR RYANODINE RECEPTOR-MEDIATED CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA

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Introduction: While rare RYR2 variants account for ~60% of clinically definite cases of catecholaminergic polymorphic ventricular tachycardia (CPVT), recent studies have suggested the rate of equally rare RYR2 variants in the general population is higher than anticipated thereby confounding the interpretation of genetic test results. Therefore, we examined the utilization of the RYR2 genetic test among referral cases and identified factors to improve interpretability.
Methods: Frequency and location comparisons were made for rare (minor allele frequency < 0.01%) RYR2 variants identified among 1355 possible to definite CPVT cases and 60,706 exomes from the Exome Aggregation Consortium (ExAC). The impact on the yield of RYR2 variants was examined for the clinical phenotype, the topological/exonic location, and predictions from five in silico tools. Probabilities of pathogenicity were derived using the frequencies in cases and ExAC controls.
Results: Only 18.2% (218/1200) of referrals hosted a putative pathogenic variant, lower than the 59% (46/78) yield among clinically definite cases, creating a much higher false positive rate among referrals considering the 3.2% background rate of rare RYR2 variants. Clearly overrepresented CPVT1 variants account for a large portion of the CPVT case yield, suggesting the next “new” RYR2 variant has a lower probability of pathogenicity than predicted. Phenotype and exonic/topologic region significantly impacted variant yield among CPVT patients. In silico tools may enhance variant interpretation but must be used with great caution.
Conclusions: While the RYR2 genetic test is considered one of the most robust genetic tests leading to strong recommendations from the current guidelines, it is clear a large majority of referral cases would not meet a classical definition of CPVT. This reduced pre-test probability leads to a potentially high false positive rate given the 3.2% background rate of benign variation. This background rate highlights the difficulty facing clinicians when interpreting genetic tests, as incorrect interpretation can lead to overzealous treatment, undue stress, and risk for the patient. Therefore, the use of clinical phenotype and exonic/topologic region can improve mutation calling.

AB40-05

CONTEMPORARY OUTCOMES IN LONG QT SYNDROME: A SINGLE CENTER EXPERIENCE

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Introduction: Long QT syndrome (LQTS) is a potentially lethal cardiac channelopathy with a registry-derived 1-5% chance/year of LQTS-triggered syncope, aborted cardiac arrest (ACA), and sudden cardiac death (SCD). We sought to evaluate the outcomes in the contemporary era from a single center.
Methods: A retrospective study comprising the 661 patients [383 females (58%), mean age at diagnosis 20 + 17 years, mean QTc 467 + 52 ms] with LQTS (LQT1 in 46%, LQT2 in 30%, and LQT3 in 8%) who were evaluated in our Genetic Heart Rhythm Clinic from 1/1999 to 7/2013. Breakthrough cardiac events (BCEs) were defined as LQTS-attributable syncope/seizures, ACA, appropriate VF-terminating ICD shocks, and SCD.
Results: In this cohort, 460 (70%) had a family history of LQTS, 285 (43%) had a family history of SCD, and there were 193 (29%) who were symptomatic prior to evaluation with an average age at first symptom of 13.9 + 12.5 years. Treatment strategies included beta-blockers in 552 (83%) and ICDs in 164 (25%) although most had arrived with their ICD already. Ninety-five patients (14%) underwent a left cardiac sympathetic denervation at our institution. With an average follow-up of 6.6 + 4.0 years, 610 patients (92%) have not experienced any LQTS-triggered BCEs events. Only 8/468 asymptomatic patients (2%) have experienced a single BCE including an ACA in a 17-year-old LQT3 female in the setting of acknowledged mexiletine non-compliance. Forty-three of the 193 previously symptomatic patients (22%) have experienced at least 1 BCE including a single BCE in 16 (8.3%). Among the 27 (4.1%) patients with > 1 BCE, 2 (compound LQT1 and LQT3) have died but both declined recommendations for treatment intensification and 3 (all LQT3) have been transplanted.
Conclusions: With careful clinical evaluation and risk assessment and after initiating a comprehensive patient-specific treatment program, nearly all asymptomatic patients ought to remain asymptomatic if compliant with their treatment program and LQTS-associated mortality should be extremely uncommon occurring in only 2 children during over 4000 patient-years of follow-up. Given that 20% of previously symptomatic patients have experienced at least 1 non-fatal recurrence, further optimization of treatment strategies should be explored.

AB40-06

NOS1AP VARIANTS AFFECTING QTC IN THE LONG QT SYNDROME- MAINLY A MALE AFFAIR?

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Introduction: Single nucleotide polymorphisms (SNPs) in the NOS1AP gene have repeatedly been reported to influence QTc, albeit with moderate effect sizes. In the long QT syndrome (LQTS) this may contribute to the substantial variance seen in QTc among carriers of identical pathogenic sequence variants. Here we assess three previously reported NOS1AP SNPs for association with QTc in two large Swedish LQT1 founder populations.
Methods: This study included 312 individuals (180 females) from two LQT1 founder populations, whereof 227 genotype positive (133 females) segregating either Y111C (n=148, 84 females) or R518* (n=79, 49 females) pathogenic sequence variants in the KCNQ1 gene, and 85 genotype negative (47 females). All were genotyped for NOS1AP SNPs rs12143842, rs16847548 and rs4657139, and tested for association with QTc length (effect size presented as mean difference between derived and wildtype, in ms). Mean QTc was obtained by repeated manual measurement (preferably in lead II) by one observer using coded 50 mm/s standard 12-lead ECGs.
Results: A substantial variance in mean QTc was seen; all genotype positive 475±33 ms (Y111C 482±30 ms; R518* 462±34 ms) and genotype negative 433±24 ms. Female sex was significantly associated with QTc prolongation in all groups ($p<0.01$) with effect sizes ranging from 14 ms (genotype negatives) to 16 ms (Y111C), 20 ms (genotype positives) and 30 ms (R518*). Two derived NOS1AP SNPs (rs12143842 and rs16847548) were significantly associated with QTc prolongation in genotype positives (10 ms, $p=0.02$), in genotype negatives similar results were seen (9 ms, $p=0.07$). Notably, among genotype positives, when stratified by sex neither of these two SNPs were significantly associated with QTc in females (all 6 ms, $p=0.2$; Y111C 9 ms, $p=0.1$; R518* 1 ms, $p=0.9$) while in males, a prolongation of 16 ms, $p=0.03$ was seen (Y111C 15 ms, $p=0.07$; R518* 27 ms, $p=0.007$). In genotype negatives, while non-significant, the same SNPs were associated with a 5 ms (females) and 10 ms (males) QTc prolongation.
Conclusions: Our findings suggest specific genotype and most importantly sex affects the effect size of NOS1AP SNPs on QTc. This may be of clinical significance when applying NOS1AP genotype to clinical risk stratification.

ABSTRACT AB41: Provocative Ablation & Interventional Cases: Potential Cutting Edge Developments

Friday, May 6, 2016
1:30 PM - 3:00 PM

AB41-01

DISAPPEARANCE OF IDIOPATHIC OUTFLOW TRACT PREMATURE VENTRICULAR CONTRACTIONS AFTER CATHETER ABLATION OF PRE-EXCITATION: A CASE SERIES

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Introduction: Multiple mechanisms have been proposed for idiopathic premature ventricular contractions (PVCs) originating from the outflow regions and aorto-mitral continuity (AMC), e.g. automaticity. Recent observations such as coexistence with pre-excitation or perinodal arrhythmias like atrioventricular nodal reentrant tachycardia (AVNRT) and the association between discrete pre-potentials and successful ablation sites of ventricular arrhythmias suggest a subset of these patients may have a different arrhythmia substrate. In this case series we present a unique syndrome that requires a combination of an

accessory pathway (AP) and PVCs from these regions.
Methods: Based on an index case referred to the cardiology department of the Erasmus Medical Center we identified a total of 10 cases from collaborating international medical centers presenting with pre-excitation in association with outflow tract PVCs on 12-lead surface electrocardiogram (ECG).
Results: All cases displayed pre-excitation and monomorphic outflow region PVCs in bigeminy or trigeminy on 12-lead ECG with fixed coupling intervals. Catheter ablation of the AP led to disappearance of PVCs in 4 cases. The site of ablation was remote from the outflow tracts. In 4 cases ablation was not undertaken and in 2 cases PVCs did not terminate after AP ablation. In most cases intermittent pre-excitation was seen, highly associated with the outflow tract PVCs.
Conclusions: Coexistence of pre-excitation with PVCs from the outflow tracts and the fact that in some cases PVCs disappeared after AP ablation together with previous findings suggests a common mechanism, which could be explained by the so-called 'dead-end tract'.

AB41-02

ELIMINATION OF BRUGADA SYNDROME PHENOTYPE BY ENDOCARDIAL ABLATION USING NOVEL MULTIPOLAR RF ABLATION CATHETER

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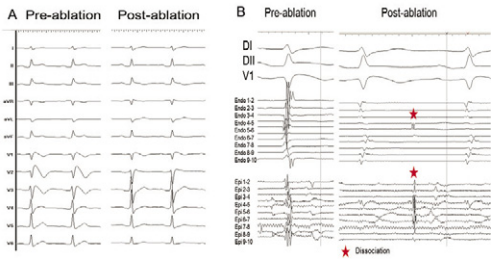
Introduction: Ventricular fibrillation (VF) is the main mechanism of sudden cardiac death in Brugada syndrome(Brs). The feasibility of eliminating BRS phenotype on 12 leads ECG by endocardial ablation using novel multipolar RF ablation has not been reported.
Methods: 3 patients with type 1 BrS(3 males,45±17years) presented with recurrent VF episodes(3±2); all had received an implantable cardiac defibrillator(ICD). Radiofrequency energy(RF) was applied simultaneously from circular irrigated multielectrode ablation atheter (nMarq) in situ using 25W during 60 seconds. Epicardial approach was undertaken for monitoring purpose. The procedural endpoint was electrical isolation of right ventricular outflow tract (RVOT)and disappearance of BrS pattern in leadsV1-V2. Outcome was assessed by clinical visit and ICD memory interrogation every 6months.
Results: Type 1 Brs was present at baseline in all with complete RBBB in one. Endocardial RVOT isolation was achieved in all using a mean of 10±4min of RF delivery with progressive delay of electrograms. It resulted in elimination of BrS in lead V1-V2 (Fig A). Importantly,RVOT dissociation was observed in one patient indicating a dead-end structure (Fig B). Epicardial monitoring demonstrated disappearance of epicardial electrogams during the course of endocardial ablation (Fig B). Over 2years of follow-up, all three patients were free of recurrent VF and permanent elimination BrS was present in all.
Conclusions: Disappearance of BrS phenotype with endocardial ablation is feasible and safe. It eliminates recurrent VF episodes at 2 years follow-up indicating a possible cure of BrS.



AB41-03

LEFT ATRIAL APPENDAGE CLOSURE GUIDED BY 3D PRINTED CARDIAC RECONSTRUCTION

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Introduction: Left atrial appendage (LAA) closure is the alternative to medical therapy in patients with atrial fibrillation (AF) and high risk of stroke or contraindication to antithrombotic treatment. 3D printing is a novel technology able to create a patient specific model of any given anatomical part. Hereby we report two cases of LAA occlusion with two different devices, the WaveCrest device (Coherex Medical, Inc., USA) and the Amplatzer Amulet device (St Jude Medical, St Paul, MN, USA), in which a 3D-printed LAA model (CareTronik, Prato, Italy) was used in a test phase for the correct device sizing and for the identification of the ideal position within the LAA vestibule.
Methods: N/A.
Results: The first patient was a 69-year-old woman with paroxysmal AF with a previous history of transient ischemic attack (TIA) despite appropriate oral anticoagulation therapy. Before device insertion in the left atrium, we tested the occlusion using the 3D model in a 27 mm WaveCrest device demonstrated a good compression and sealing confirming the correct sizing. The first position revealed an uncovered proximal lobe; after careful retraction, a more proximal position was obtained, replying the one obtained during the "fitting" test phase, allowing a complete covering of the proximal lobe as well. The second patient was a 42-year-old man with persistent AF referred for LAA occlusion due to a TIA despite adequate warfarin therapy. The diameter of the LAA "neck" was 23-25 mm at the landing zone and 28 mm at the ostium. A first attempt with the 27 mm Amulet device, delivered within the 3D printed LAA, revealed insufficient covering of the proximal part of LAA vestibule; a second test with the 31 mm Amulet demonstrated a good sealing: the correct sizing was thereafter confirmed by color-Doppler TEE showing complete sealing. No procedural-related complications occurred in both cases.
Conclusions: Many variables need to be considered to accurately select the device which best fits the LAA size and morphology. In the first case the 3D model helped in finding the correct position to cover a proximal LAA lobe, while in the second case it was useful to choose the correct size of the device, guiding the choice of the largest Amulet despite the measurements provided by angiography and TEE.

AB41-04

ELIMINATION OF VENTRICULAR ARRHYTHMIA IN CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA BY TARGETTING "CATECHOLAMINE-SENSITIVE AREA": A CASE REPORT

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Introduction: Reports of successful catheter ablation of ventricular arrhythmia in catecholaminergic polymorphic ventricular tachycardia (CPVT) are rare, and the mechanism for bidirectional ventricular premature contractions (VPCs)/VT are still unknown.
Methods: N/A.
Results: We report on a 24-year-old female diagnosed with CPVT by genetic testing who had been suffering from multiple episodes of syncope associated with exercise since childhood. Treadmil exercise testing induced bigeminal VPCs with right bundle branch block (RBBB) configuration and inferior axis as well as bidirectional VPCs, both of which were highly symptomatic. We performed catheter ablation of VPCs induced by epinephrine infusion. VPCs were classified roughly into 3 types: type 1 and type 2 VPCs showed RBBB configuration and inferior axis, and type 3 VPCs showed RBBB configuration and superior axis. Interestingly, type 3 VPCs (superior axis) always immediately succeeded type 1 or type 2 VPCs (inferior axis). Type 1 and Type 2 VPCs were eliminated by radio frequency (RF) applications at the left aortic sinus of Valsalva and the vicinity of the anterolateral papillary muscle, respectively. And after the elimination of inferior axis type 1 and 2 VPCs, no spontaneous VPCs were seen even during high dose epinephrine infusion. However, pacing resulting in capture at the anterolateral papillary muscle where ablation was successful for type 2 VPCs induced type 3. This phenomenon was observed reproducibly, and we performed RF applications for type 3 VPCs at the left ventricular inferoseptal area where good pace mapping was obtained. Treadmill testing after the ablation induced no VPCs or VT at the maximal workload, and the patient has been asymptomatic for 1 year.
Conclusions: The electrophysiological findings in our case have important implications both for understanding the pathophysiology of CPVT and for suggesting therapeutic strategies.

AB41-05

CONCOMITANT EPICARDIAL AND ENDOCARDIAL ELECTROANATOMIC VOLTAGE MAPPING OF AF DURING HYBRID ABLATION

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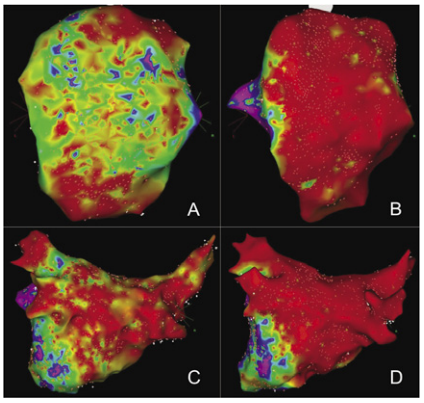
Introduction: The management of persistent atrial fibrillation (PeAF) remains elusive. The Convergent technique coupled with cryoballoon pulmonary vein isolation (PVI) is an alternative to catheter or surgical approaches. We report for the first time high density electroanatomic mapping performed in the pericardium before and after epicardial (EPI) ablation and endocardial (ENDO) mapping before and after ENDO ablation of the posterior left atrium (pLA) as well as near simultaneous EPI and ENDO maps following EPI ablation.
Methods: N/A
Results: The patient is a 62 year old female with long standing PeAF. An EPI ablation of the pLA was performed using a novel pericardioscopic approach utilizing the Epi-Sense RF catheter. Panel A shows the pLA epicardium mapped within the pericardial space at a voltage between 0.01mV to 1.0mV while in AF. The voltage map shows a heterogenous area extending from the superior pericardial reflection to coronary sinus. The inferior margin shows voltage attenuation which reflects EPI fat insulating the coronary sinus and annulus. Panel B shows the EPI pLA mapped after EPI ablation and endocardium (Panel C) following EPI ablation. The pLA is silenced after cryoballoon PVI (Panel D) suggesting activity seen in the pLA after EPI but before ENDO ablation is far field or receives electrical inputs from the pulmonary vein antrum.
Conclusions: The Convergent procedure with cryoballoon ablation is an effective means of ablating the pLA more safely and effectively than stand alone ENDO or surgical ablation. Electrograms in the pLA were undetectable at the lowest sensitivity from an EPI or ENDO approach suggesting an effective method of achieving transmurality.



AB41-06

SINUS NODAL DYSFUNCTION CAUSED BY CIRCUMFERENTIAL PULMONARY VEIN ABLATION: LESSONS FROM LATE GADOLINIUM ENHANCEMENT CARDIOVASCULAR MAGNETIC RESONANCE IMAGING

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Introduction: Severe sinus node (SN) dysfunction is a rare and unexpected complication of RF ablation in the left atrium (LA). As potential mechanism, thermal injury to the SN artery has been proposed.
Methods: N/A.
Results: A 54-year old male was referred for circumferential pulmonary vein (PV) ablation. The procedure was carried out in sinus rhythm and during deep sedation, utilizing a 3D mapping system in conjunction with an integrated CT image of the LA. We used an open-irrigated ablation catheter and a circular mapping catheter. With completion of the right circumferential line at the antero-superior LA (outside the right superior PV) (A*), a sudden decrease in sinus rate (B) was noted. Atrial pacing was initiated, while surface ECG provided no evidence for acute myocardial ischemia. After the procedure, slow junctional escape rhythm persisted (C). After 5 days, the escape rhythm persisted at rest and during exercise. Cardiovascular magnetic resonance imaging (cMRI) demonstrated enhanced signal intensity in the anterior right atrial wall at the superior cavoatrial junction

(D, short axis view), indicating edema (e. g. ischemic) at the SN region. Thirteen days post ablation, normal sinus rhythm recurred. Chronotropic incompetence initially persisted but resolved during later follow-up.

Conclusions: Severe SN dysfunction can result from circumferential PV ablation. Our findings form cMRI provide evidence for SN ischemia as the underlying mechanism. Of note, delayed recovery of SN function should be considered prior to permanent pacemaker implantation.