

nection between the right AV ring and the apex of the RV was present, bypassing the AV-node. There was lack of expression in the RV inflow tract, which may be in accordance with the secondary addition of myocardium to this area.

**Conclusion:** Lac Z reporter gene expression is able to delineate the developing murine cardiac conduction system. Next to the CCS-lacZ expression in the right and left AV ring, expression was observed in the right ventricular moderator band, which was connected to the right AV ring. These findings may implicate a developmental morphological substrate for WPW-syndrome and Mahaim tachycardias.

Noon

1001-18

### Determinants of Natural Regression of Pulmonary Vein Stenosis Secondary to Radiofrequency Catheter Ablation for Atrial Fibrillation

**Yong-Mei Cha,** samuel J. Asirvatham, Thomas M. Munger, Paul A. Friedman, Luiz Leite, Laura Peterson, Christie Bluhm, Douglas L. Packer, Mayo Clinic, Rochester, MN

**Background:** Pulmonary vein (PV) stenosis following radiofrequency ablation (RFA) for the treatment of trigger-mediated atrial fibrillation (AF) may undergo spontaneous regression in some cases. The conditions favoring this change are unclear however. **Methods:** Therefore, the determinants of spontaneous reversal of RFA-mediated PV stenosis was studied in 203 consecutive patients (pts) who underwent ablation of 525 PVs for drug-refractory paroxysmal AF. Three-dimensional reconstructions of 8 or 16 row spiral CT images were utilized to measure the narrowest, cross-sectional diameter of the PVs at baseline (B), 3-month (3M) and >6-month (6M) after RFA. **Results:** Moderate PV stenosis (>50%) developed in 11 pts (17 PVs) following the ablation. Significant reduction of PV stenosis was observed in 4 pts. (6 PVs) at >6-months of follow-up (group 1: 15±2mm at B; 6±1mm at 3M; 9±2mm at 6M; p<0.05). In contrast, the severity of PV stenosis remained unchanged or worsened in the other pts (group 2: 12±2mm at B; 4±2mm at 3M; 2±1mm at 6M). Univariate analysis revealed predictors of spontaneous reduction of PV stenosis as shown in the table. The baseline PV size was the most important predictor, while age, AF duration, number of RF delivery, duration and temperature of RFA were not predictive of outcome. **Conclusion:** Despite >50% narrowing after RFA, spontaneous remodeling occurs in the PVs with largest baseline diameter. Ablation duration and temperature are less important determinants of the long term outcome of PV stenosis.

	Chi-Square	P value	Odds Ratio	Confidence Interval
Age	0.06	0.80	0.99	0.91-1.08
AF duration	0.36	0.55	0.93	0.74-1.10
Baseline PV diameter	3.89	0.04	2.24	1.01-4.98
Number of RF delivery	2.49	0.11	0.90	0.79-1.03
Duration of RFA	2.04	0.15	0.96	0.91-1.02
RFA temperature	0.07	0.79	0.96	0.71-1.29

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### Optimal Catheter Ablation Strategy for Atrial Fibrillation: Trigger Isolation Alone or Supplementary Left Atrial Substrate Modification?

**Dipen Shah,** Haran Burri, Henri Sunthorn, Ulrich Sigwart, Hôpital Cantonal Universitaire de Geneve, Geneva, Switzerland

#### Background

Selecting the minimum effective intervention for curative ablation of atrial fibrillation (AF) may reduce side effects. We evaluated pulmonary vein (PV) trigger isolation vs supplementary left atrial (LA) substrate modification in a consecutive cohort of patients with AF. **Methods**

58 patients (45M,13 F; age 55 ± 9 yrs; 4 with structural heart disease) underwent curative catheter ablation for drug resistant, symptomatic paroxysmal (n=42) or persistent AF (n=16). Irrigated tip RF ablation was used to perform circular mapping guided electrogram demarcated isolation of all PVs (35 W limit), cavotricuspid isthmus ablation and linear LA ablation (50W limit) guided and validated by Biosense 3D mapping.

#### Results

Successful isolation of all PVs (n=230) was performed in all patients. Cavotricuspid isthmus block was created in 32 patients with typical atrial flutter and linear LA ablation performed in 14 patients with either persistent AF (n= 10) or recurrent AF despite successful PV isolation (n= 4). Linear ablation from the left PV ostia to the mitral annulus was performed in 14 (complete block in 11), and across the posterior LA from the right to left ostia in 7 (block in 3). 1.4 procedures per patient (187± 51min, RF time 39 ± 14min) were performed: (1.2 procedures per paroxysmal AF patient). One reversible ischemic neurologic deficit and one tamponade occurred. After a follow up of 9 ± 5 months, with 6 patients on antiarrhythmic drugs (AAD), 1 patient has persistent LA flutter and 2 have paroxysmal AF, so that 95% (40/42) with paroxysmal AF and 72% (12/16) with persistent AF are in stable sinus rhythm without AAD.

#### Conclusion

Electrogram demarcated circular mapping guided isolation of all PVs (often supplemented by cavotricuspid isthmus ablation) results in excellent drug free success rates in patients with paroxysmal AF without requiring additional LA linear ablation. High success rates may be achieved in patients with persistent AF when PV isolation is supplemented by electrophysiologically validated linear LA ablation.

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### Investigation of Coronary Venous Anatomy by Multislice Computed Tomography

**Jing Ping Sun,** Neil J. Greenberg, Bruce L. Wilkoff, Craig R. Asher, Richard D. White, James D. Thomas, Mario J. Garcia, The Cleveland Clinic Foundation, Cleveland, OH

**Background:** The coronary venous system is increasingly being targeted for left ventricular or biventricular pacing in patients with severe heart failure. The present study investigated the appearance of the coronary sinus and its tributary veins as visualized on multi slice computed tomography (MSCT) in patients with coronary artery disease (32), chest pain (9), valvular disease (5) and hypertrophic cardiomyopathy (2).

**Methods and Results:** Forty-eight patients (60±10 years old, 38 males) were scanned using a retrospectively ECG-tagged cardiac protocol on a 16-slice CT scanner. The scan was initiated following intravenous contrast agent administration and enhancement of the aorta. The entire heart was imaged within a single breath-hold. CT scan parameters included: 140 kVp, 400 mAs, 0.8 mm slice thickness, 0.4 mm slice increment, 0.42 sec rotation time, 0.2 - 0.3 pitch. The appearance of coronary venous segments was evaluated using volume renderings in three-dimension space. The diameter, length, and angulation of coronary veins were measured from curved multi-planar reformatted images following vessel centerline extraction. The characteristics of coronary veins are listed in the table.

	Coronary Sinus	Middle Middle	Posterior	Lateral	Anterior	Posterior-lateral	Anterior-lateral
Ostial Diameter (mm)	9.3±2.7	4.6±1	3.6±0.7	3.0±0.8	3.7±0.6	3.2 ±1.2	2.5±0.9
Length (mm)	110±22	51±22	42±26	34±24	49±16	40±35	25±15
Take-off angle		77±21	94±29	113±22	123±27	112±20	90±38
Appearance (%)	100	90	75	70	70	30	20

**Conclusions:** This study shows the appearance, diameter, length, and angulation of coronary veins can be determined using MSCT. This capability should be useful for pre-operative lead placement planning in the coronary venous system.

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### Inhibition of ERK/p38 MAP-kinase and Calcineurin-NFAT Hypertrophy Signaling by Inducible Hemoxygenase-1 in Cardiac Myocytes

**Joern Tongers,** Beate Fiedler, Tibor Kempf, Theresia Kraft, Stepan Gambaryan, Suzanne M. Lohmann, Kai C. Wollert, Hannover Medical School, Hannover, Germany, University of Würzburg, Würzburg, Germany

Inducible hemoxygenase-1 (HO-1) is the rate-limiting enzyme of heme degradation, and promotes the formation of carbon monoxide (CO), free iron, and biliverdin (BV), which is continuously converted to bilirubin (BR) by biliverdin reductase. HO-1 has previously been shown to protect cardiac myocytes (CM) from ischemia/reperfusion injury. We postulated that HO-1 and its reaction products may, in addition, promote anti-hypertrophic effects in CM. Endothelin-1 (ET-1, 30nmol/L) promoted increases in cell size (planimetry), sarcomere organization (confocal laser microscopy), and ANP expression (Northern blot) in ventricular CM isolated from 1-3 day-old rats. Adenoviral overexpression of HO-1 (Ad.HO-1), but not LacZ (not shown), significantly reduced this hypertrophic response. The effects of Ad.HO-1 were mimicked by the CO-donor [Ru(CO)<sub>3</sub>C<sub>2</sub>H<sub>2</sub>], BV, and BR (5µmol/L, each), suggesting that CO and BV/BR both contribute to the antihypertrophic effects of HO-1 (Table). As shown by immunoblotting using phospho-specific anti-MAP-kinase antibodies, CO and BV/BR suppressed the activation of ERK1/2 and p38 by ET-1. As revealed by NFAT-luciferase reporter assays, CO and BV/BR also inhibited the calcineurin-NFAT signaling pathway in ET-1 stimulated CM. In conclusion, HO-1, via formation of CO and BV/BR, promotes anti-hypertrophic effects in CM that are mediated, at least in part, via inhibition of ERK/p38 MAP-kinases and the calcineurin-NFAT signaling pathway.

Mean ± SEM, \*p<0.05 vs. ET-1, n=3-8 experiments

	Control	ET-1	ET-1 + Ad.HO-1	ET-1 + CO	ET-1 + BV	ET-1 + BR
Cell size	100	175 ± 18	113 ± 8	138 ± 12*	135 ± 9*	134 ± 9*
Sarcomere organization	100	160 ± 7	n.d.	122 ± 7*	127 ± 7*	n.d.
ANP mRNA	100	698 ± 173	308 ± 86*	323 ± 100*	192 ± 51*	232 ± 55*