SPECT and FDG SPECT on the same day; the early Tl-201 image obtained in the RR protocol was also used as a perfusion study for comparison with FDG SPECT. The SPECT data were analyzed semiquantitatively using circumferential count profiles, and displayed in polar maps (13 segments). For the FDG/Tl-201 SPECT approach, segments were classified as viable when showing normal perfusion or ≥ 7% increased FDG uptake in perfusion defects (mismatch). For Tl-201 RR SPECT, criteria for viability were both the percentage of Tl-201 uptake and reversibility of defects on the redistribution image. Of 312 analyzed segments, 113 had abnormal wall motion at baseline and 106 were revascularized. Recovery of function was observed in 36 segments, whereas 70 segments did not improve. FDG/Tl-201 SPECT showed sensitivity of 86% (31/36) and a specificity of 77% (54/70) to detect functional recovery. Tl-201 RR SPECT had a sensitivity of 78% (28/36) and a specificity of 59% (41/70). Stepwise logistic regression showed that FDG/Tl-201 SPECT was the single best predictor for functional recovery after revascularization. In conclusion, the data suggest that FDG/Tl-201 SPECT is superior over Tl-201 RR SPECT in the identification of segments capable to improve in function after revascularization.

789 Atrial Defibrillation

Wednesday, March 27, 1996, 10:30 a.m.–Noon
Orange County Convention Center, Room 222

10:30

789-1 Video Imaging of Atrial Fibrillation and Defibrillation in the Isolated Langendorff-Perfused Sheep Heart

Richard A. Gray, Gregory M. Ayers[1], José Jalife. *SUNY Health Science Center at Syracuse, NY;[1] InControl, Inc, Redmond, WA*

The effects of defibrillatory shocks on the organization of electrical activity during atrial fibrillation (AF) have not been previously studied. In addition, the reason why some shocks fail and others are successful remains unclear. We have studied the events that precede, accompany and follow the application of successful, as well as unsuccessful atrial defibrillatory shocks. To this aim, we have used high resolution video imaging to record transmembrane potentials simultaneously from over 20,000 sites on the epicardial surface of the right and left atrium of the Langendorff-perfused sheep heart (sampling rate was either 120 or 240 frames/sec). We constructed isochrone maps during sinus rhythm and during AF, as well as following shocks applied by a programmable atrial defibrillator. During AF, complete reentrant circuits were never observed for more than one beat. In addition breakthrough patterns of activity were often seen. These results indicate that AF is not a two-dimensional phenomenon, but involves transmural propagation. Biphasic shocks (1.2 ± 0.6 J; n = 6) were delivered through electrodes placed in the right atrium and the coronary sinus. These shocks depolarized all epicardial regions of the atria and resulted in four types of responses: 1) immediate cessation of epicardial activity, 2) a single post-shock activation, 3) organized activation for 0.8–1.5 seconds followed by termination, and 4) organized activity followed by degeneration back into AF. Types 2–4 involved a quiescent period lasting 110 ± 28 ms immediately following the shock, then an activation sequence similar to those observed during sinus rhythm. The first cycle length after the shock for types 3 and 4 (170 ± 36 ms) was longer than during AF (144 ± 33 ms). These results indicate that the shock depolarized the entire atrial epicardial surface followed by a quiescent period after which organized activation emanated from the sinoatrial pacemaker region. These results are consistent with the "upper limit of vulnerability" hypothesis.

10:45

789-2 Is It Safe to Deliver Internal Atrial Defibrillation Shocks During Single Vessel Myocardial Ischemia?

Xavier Gonzalez, Gregory M. Ayers, Marina B. Ilina, Darrell O. Wagner, William A. Strokman, Clif A. Alferness. *InControl Inc. Redmond, WA*

Previous work has shown delivery of synchronized low energy internal atrial defibrillation shocks to terminate atrial fibrillation. We tested the safety of this procedure in association with single vessel myocardial ischemia (SVMI) and re-perfusion.

Methods: In six isofluorane anesthetized sheep (53 ± 9 kg) two leads each with a 6 cm distal shocking coil were positioned, one in the coronary sinus and one in the right atrium. A bipolar pacing lead was positioned at the right ventricular apex for shock synchronization. An atrial defibrillation threshold (ADFT) was determined before SVMI. A balloon angioplasty catheter was inflated to occlude the circumflex (CX) artery. Each minute after inflation, AF was induced and a shock was delivered at ADFT, two times ADFT if the AF persisted and a 300 V shock independent of AF termination. The procedure was continued for 15 minutes or until severe ischemia related arrhythmias or hemodynamic changes were seen. When the balloon was deflated, shocks were delivered for the same length of time. After electrocardiographic and hemodynamic recovery, the procedure was repeated in the left anterior descending (LAD) artery. *Results:*

Groups	N	# Shocks in AF	% Success	# Shocks in NSR
CX inflated	6	76	57	47
CX deflated	6	44	48	35
LAD inflated	5	41	49	27
LAD deflated	5	30	77	31

A total of 331 shocks were delivered during SVMI and re-perfusion. None of these shocks produced ventricular tachycardia or fibrillation. AF was terminated in 63% of episodes. Three episodes of VF not associated with shocks were seen immediately after balloon deflation. *Conclusions:* In this model, SVMI does not appear to negatively impact the safety of internal atrial defibrillation.

11:00

789-3 Safety of Atrial Defibrillation: The Importance of Pre-Shock R-R Intervals and the Risk of Premature Ventricular Contractions

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Premature ventricular complexes (PVC) are not uncommon in patients with atrial fibrillation (AF). The risk of ventricular fibrillation (VF) induction by atrial defibrillation shocks synchronized or coupled with a PVC remains unknown and is a great concern for the potential application of implantable atrial defibrillators. We determined the safety of internal atrial defibrillation shocks (0.8–3.0 J, 3/3 ms biphasic) during AF by selectively synchronizing or coupling the shock with the short R-R intervals (< 300 ms) of normal QRS complexes and simulated PVCs respectively. AF was produced by chronic atrial pacing (400 beats/min × 4 weeks) in 11 dogs. The short R-R interval was selected using a computer system at the baseline and during isoproterenol infusion (2 mcg/min). Of the 872 shocks with pre-shock R-R interval < 300 ms (243 ± 19 ms), not one induced VF in any dog. However, when a shock was synchronized with simulated PVCs of various coupling intervals (normal QRS-shock coupling), VF was induced in all dogs. The longest normal QRS-PVC/shock interval at VF induction was 186 ± 33 ms (145–270) and the VF induction window (the diastolic interval during which VF was inducible) was 34 ± 11 ms (20–60). When a shock of various timing followed a preceding PVC (PVC-shock coupling), VF was induced over a much wider time window (34 ± 11 vs 124 ± 27 ms, $p < 0.01$) in all dogs. The longest shock coupling interval (PVC-shock interval) at VF induction was extended from 186 ± 33 to 270 ± 30 ms (range 220–320, $p < 0.01$).

Conclusions: (1) Synchronized atrial defibrillation is safe during AF with short R-R intervals if the QRS are all normal. (2) To avoid synchronizing a shock with a PVC and the QRS complex immediately following the PVC may further improve the safety of internal atrial defibrillation.

11:15

789-4 Which Patients Do Benefit From an Implantable Atrial Defibrillator?

Werner Jung, Dietrich Pfeiffer, Christian Wolpert, Luciano Pizzulli, Wolfgang Fehske, Burghard Schumacher, Thorsten Lewalter, Heyder Omran, Thomas Korte, Berndt Lüderitz. *Department of Cardiology University of Bonn, Bonn, Germany*

External cardioversion has been an effective and safe method for termination of atrial fibrillation. Low-energy endocardial cardioversion has been suggested as an alternative approach. We report our experience with internal atrial defibrillation in 11 consecutive patients (pts) with paroxysmal (n = 4 patients) or chronic (n = 7 patients) atrial fibrillation. Biphasic shocks were synchronized with the R wave and delivered between transvenous catheters located in the right atrial appendage and the coronary sinus. The energy of the initial shock was 0.5 J and incremented by 0.5 J steps up to a maximum of 5 J. Thereafter repeated shocks were delivered with 5 J increments until successful conversion. All patients were asked to report pain perception after each shock delivery.

Results: 4 patients suffered from lone atrial fibrillation and 7 patients had a structural heart disease. Mean left atrial diameters were 45 ± 4 mm. Duration of atrial fibrillation lasted from 5 days to 450 days (mean 180 ± 130 days). Internal atrial defibrillation was effective in all patients. The mean atrial defibrillation threshold was 9.6 ± 6.8 J (range from 0.5 J to 20 J). No ventricular arrhythmias were induced and no other complications occurred. 8

of 11 (73%) patients indicated that shocks ≤ 1 J were painful and all required sedation at a shock energy level > 2 J.

Conclusions: (1) Internal atrial defibrillation could be safely and effectively performed in all patients in this series. (2) However, only in 36% of the patients atrial fibrillation could be terminated with an energy ≤ 3 J. Thus, only a minority of patients may benefit from an implantable atrial defibrillator capable of storing a maximum shock energy of 3 J. (3) Pain perception may have a major impact on quality of life in patients with an implantable atrial defibrillator since the majority of the patients (73%) reported severe pain at shock energies < 1 J.

11:30

789-5 Safety of Transvenous Atrial Defibrillation in Patients With Monomorphic Ventricular Tachycardia and Heart Disease

Andrea Natale, Margaret M. Kearney, M. Joan Brandon, Mary J. Geiger, Helen Barold, Gery Tomassoni, Virginia Kent, Keith H. Newby. *VA Medical Center/Duke University, Durham, NC*

History of ventricular tachycardia (VT) and depressed ejection fraction may affect transvenous atrial defibrillation (AD) increasing the likelihood of shock-related arrhythmias. In 25 pts with VT (mean age 65 ± 8 years; EF 29 ± 9%) we assessed the safety of AD using 2 catheters in the right atrial appendage and coronary sinus. In each pt, AD was performed with increasing energy starting at 0.5 joules. The protocol was performed both in drug free state and during isoproterenol infusion. In 5 pts AD was attempted during VT and atrial pacing with AV conduction at the same rate of VT. Shocks were synchronized using a Medtronic external defibrillator model 2394. A total of 398 shocks were analyzed. No ventricular tachyarrhythmias were observed after shocks synchronized on the R wave. In 3 pts ventricular fibrillation followed inappropriate shocks on the T wave. In all 3 pts, T wave shocking was seen only during isoproterenol infusion. Shocks delivered during VT always resulted in acceleration of VT (1 pt) or degeneration to VF (4 pts). However in the same pts shocks during atrial pacing with ventricular rate similar to VT did not induce ventricular arrhythmias. In conclusion: 1) In pts with VT transvenous atrial defibrillation is safe when shocks are properly synchronized. 2) Atrial defibrillation during VT appears proarrhythmic. 3) Whether isoproterenol infusion increases the likelihood of inappropriate T wave oversensing needs further evaluation.

11:45

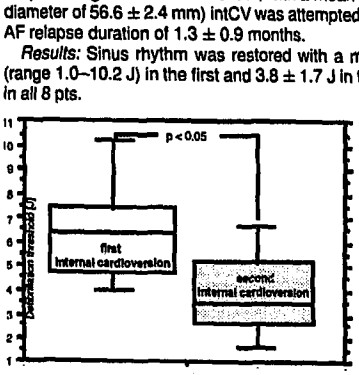
789-6 Repeated Internal Low-Energy Cardioversion of Atrial Fibrillation

Eckhard Alt, Richard Ammer, Claus Schmitt, Jay Pasquantonio, Fred Evans. *I. Med. Klinik, Klinikum rechts der Isar, Technical University München, Germany*

Background: The goal of this study was to determine if repeated internal cardioversion (intCV) of atrial fibrillation (AF) required the same energy for conversion as previous successful intCVs.

Methods: IntCV was successfully performed in 51 of 56 pts by delivering 3 ms/2 ms biphasic shocks (Ventritex HVS 02, Sunnyvale CA) between two custom-made intracardiac electrode catheters (6F, Elecath Inc., Rahway NJ). The shocks were R-wave triggered, voltage was increased by 40V per shock in intervals until sinus rhythm was achieved. Pts were sedated with Midazolam. After a mean follow-up of 11 ± 6 months, 20 pts experienced a second episode of AF. In 8 of these pts (age 59 ± 10 years, initial episode AF persisting for 7.1 ± 2.5 months, with a mean left atrial echocardiographic diameter of 56.6 ± 2.4 mm) intCV was attempted a second time after a mean AF relapse duration of 1.3 ± 0.9 months.

Results: Sinus rhythm was restored with a mean energy of 6.4 ± 2.1 J (range 1.0–10.2 J) in the first and 3.8 ± 1.7 J in the second intCV ($p < 0.05$) in all 8 pts.



Conclusions: Repeat intCV requires less energy than primary intCV of chronic AF given that the second episode is of shorter duration than the first. A large number of pts are ineligible for atrial defibrillator implantation due to atrial defibrillation thresholds (DFTs) exceeding the acceptable pain level. This study implies that such pts would have considerably lower DFTs, and as a result less pain, if their AF was quickly detected and addressed, such as in the case of an implanted atrial defibrillator. Therefore, these pts may indeed be suitable candidates for atrial defibrillator implantation.

790 Nitric Oxide: Physiology, Pharmacology, and Pathology

Wednesday, March 27, 1996, 10:30 a.m.–Noon
Orange County Convention Center, Room 208

10:30

790-1 In Vivo Nitrate Tolerance Is Not Associated With Decreased Production of Nitric Oxide

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Reduced bioconversion of nitroglycerin (NTG) to nitric oxide (NO) is regarded as a major contributor to the development of nitrate tolerance (Tol). However, the validity of this hypothesis has not been examined. We measured production of NO in vascular tissues from nitrate tolerant and non-tolerant rats by in vivo spin-trapping of NO. Conscious rats received an i.v. infusion of NTG (1 mg/hr, Tol + NTG group, (n = 8)) or NTG vehicle. (placebo + NTG group, (n = 8)) for 72 hrs and NO was trapped by dieethyldithiocarbamate (DETC) and Fe^{2+}-citrate during an additional final 20-min infusion of NTG (6.5 mg/kg). Baseline NO production was measured in another group of rats not treated with NTG (n = 8, control). Tolerance was documented after 72 h. by an 83% reduction in the hypotensive response to a NTG bolus (From 24 ± 3 (0 hrs) to 2 ± 1 mmHg (72 hrs); $p < 0.05$). Tissues were removed and analyzed for $NOFe(DETC)_2^2$ complexes by ESR spectroscopy. Data are presented as nmol NO/g tissue/20 min.

Mean (± Sem)	Aorta	V. cava	Heart	NTG Responses (mm Hg)
Tol + NTG	1.8 ± 0.3	2.2 ± 0.3	5.1 ± 0.5	24 ± 3 vs 2 ± 1
Placebo + NTG	0.9 ± 0.2	1.2 ± 0.2	1.7 ± 0.2	25 ± 3 vs 2 ± 1
Control	0 ± 0	0 ± 0	0.2 ± 0.01	27 ± 3

The results suggest that the amounts of NO produced from NTG in hemodynamically nitrate tolerant rats (TOL ± NTG) are higher or similar to the amounts of NO produced in non tolerant rats (placebo + NTG, $p < 0.05$). It is concluded that the in vivo NTG tolerance is not caused by a reduced bioconversion of NTG to NO. Instead, tolerance may be associated with a reduction of the biological activity of NO.

10:45

790-2 Antiplatelet Effect of Nitroglycerin Is Primarily Mediated by Glutathione-s-Transferases in Human Plasma

Liying Chen, Jawahar L. Mehta. *University of Florida, Gainesville, FL; VA Medical Center, Gainesville, FL*

Current hypothesis relative to the mechanism of action of NTG involves metabolic activation of NTG to nitric oxide (NO) by glutathione-s-transferases (GST). Whereas GST metabolizes organic nitrates in the liver, it is unclear if these enzymes are present in human plasma or platelets, and are involved in the antiplatelet effects of NTG. We investigated the role of GST in the inhibition of platelet aggregation by NTG. Different concentrations of NTG (1–100 μg/ml) were incubated with platelet-rich plasma or washed platelet suspension, and aggregation induced by ADP or thrombin. NTG caused a concentration-dependent inhibition of platelet aggregation in platelet-rich plasma with $IC_{50} \approx 50$ μg/ml. The aggregation inhibitory effect of NTG was not observed in washed platelet suspension. In contrast, authentic NO caused about 50% decrease in aggregation in washed platelet suspension. The aggregation inhibitory effect of NTG in platelet-rich plasma was oxyhemoglobin (Hb)-sensitive. The aggregation inhibitory effect of NTG in platelet-rich plasma was potentiated by propylthiouracil (600 μg/ml), a GST inducer, and antagonized by ketoprofen (100 μg/ml), a GST inhibitor. These phenomena were not observed in washed platelet suspension. Since Hb cannot penetrate platelets, reversal of the effect of NTG by Hb must have been due to removal of NO from the extracellular medium. This concept was confirmed in other studies, wherein NTG (100 μg/ml) increased nitrite levels 3 fold in platelet-rich plasma after 60 min incubation. On the other