

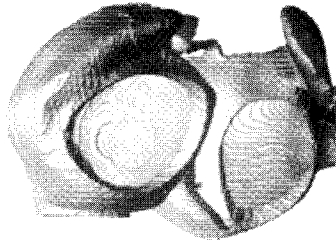
ABSTRACT SESSION 11: BASIC SCIENCE IV: Scrolls, Alternans and Fibrillation  
Friday, May 10, 2002, 8:00 AM - 9:30 AM

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**The Effect of Electrical Restitution on the Stability of Scroll Wave Reentry in Simulated Human Atrium**

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Using the Courtemanche-Nattel human atrial cell model, we have found that the stability of spiral wave reentry in 2-D simulated atrial tissue is well-predicted by the slope of the effective refractory period (ERP) restitution curve. Whether this holds true in a 3-D anatomically-realistic model of the human atrium has not yet been demonstrated. In this study, four phenotypes of spiral wave reentry (break-up, hyper-meandering, meandering and stable) were created in 2D homogeneous tissue by reducing the maximum conductance of the L-type calcium current (gCaL) to progressively flatten the slope of ERP restitution. We then examined the effect of the complex anatomy of the whole human atrium on the stability of these four phenotypes by initiating a scroll wave in the right atrium and observing the behavior. We found that 1) When the slope of ERP restitution was  $< 1$  for all diastolic intervals (DI), the initiated scroll wave was sustained, and either remained stationary or meandered. 2) If the slope of ERP restitution was  $> 1$  over a narrow DI range, the initiated scroll wave meandered chaotically, but could only sustain several rotations before extinguishing at a boundary (Figure). 3) When the slope of ERP restitution was  $> 1$  over a wide range of DI corresponding to the breakup phenotype in 2D, scroll wave breakup failed to occur because the scroll wave meandered to a boundary and extinguished before enough time had elapsed for breakup to occur. This may explain why only non-sustained atrial fibrillation can typically be induced in normal human atrium.

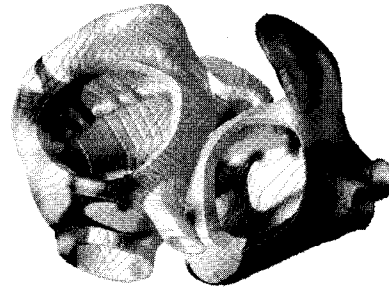


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**The Role of Decreased Conduction Velocity in the Initiation and Maintenance of Atrial Fibrillation in a Computer Model of Human Atria**

Elizabeth M. Cherry, PhD, Flavio Fenton, PhD, Harold M. Hastings, PhD, Fagen Xie, Alan Garfinkel, James N. Weiss and Steven J. Evans. Hofstra University, Hempstead, NY, Beth Israel Medical Center, New York, NY and UCLA School of Medicine, Los Angeles, CA.

Decreased electrical conduction is important in the development of a substrate for chronic atrial fibrillation (AF) and may be a necessary condition for the initiation of AF. To test this hypothesis, we analyzed the behavior of simulated atrial fibrillation in an anatomical model of human atria that included bundles like the crista terminalis and the pectinate muscles with faster conduction velocity (150-200 cm/s) than bulk tissue (60-75 cm/s) under normal conditions. The ionic model used was based on the Courtemanche et al. model of human atrial action potentials, with parameter values describing the physiology of both normal atrial cells and cells that have undergone AF-induced electrophysiological remodeling (reduced outward  $K^+$  and L-type Ca currents). We found that fibrillation initiated through reentrant spiral waves or ectopic foci was not sustained in this anatomical model for normal (non-AF) or altered (AF) electrophysiology. However, decreasing conduction velocity in bulk tissue by 30% (to 40-55 cm/s) allowed AF to be sustained, even when using normal (non-AF) electrophysiological parameters (although the average cycle length obtained using non-AF parameters was longer than observed clinically). Our findings suggest that conduction velocity abnormalities may be more important than cellular electrophysiological remodeling during the development of chronic AF.



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**Effect of Myocardial Fiber Structure and Ventricular Wall Curvature on 3-Dimensional Reentry**

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Reentry in the thick ventricular wall organizes in scroll waves around a tornado-like core called "filament". Usually reentry is hidden under the epicardium and filaments are parallel to the surface. We studied the effect of myocardial fiber structure and wall curvature on the dynamics of such filaments. We hypothesized that the curvature of the ventricular wall pulls intramural filaments toward the endocardium but that this may be counterbalanced by the fiber organization. Methods: We considered a 15 mm thick wall of a cylindrical ventricle with a transmural 120 deg twist in fiber direction and an intramural scroll with a circumferential filament that surrounded the cavity. Symmetry allowed implementation of such a model in a 2-dimensional sheet representing a radial section of the 3-dimensional curved wall. Fibers' twist was set in such a way as to have the circumferential fibers (rings) in the subepicardium. The kinetics of the cells was of the FitzHugh-Nagumo type and the scroll was always initiated with its filament in the midmyocardium. Results: The filaments could either stabilize in the myocardium or disappear at the endocardial surface, depending on the size of the cavity. As the ventricle became smaller and its wall curvature increased, the centripetal effect strengthened. When the endocardial radius (R) was larger than ~9 mm, the influence of fiber organization was larger than that of curvature, which caused the filament to drift outward toward the epicardium and stabilize in the layer with the circumferential fibers. When R became smaller than ~9 mm the influence of the curvature became comparable with that of fiber organization and the filament remained around its initial myocardial depth. Only when R was made smaller than ~1 mm the filament drifted toward the cavity center and the scroll terminated on the endocardial boundary. Conclusion: The myocardial fiber structure can counterbalance the tendency of an intramural curved filament in the wall to collapse. It is predicted that the base of the ventricles, where wall curvature is small, is more prone to have stable intramural reentrant waves aligned with fibers than the apex.

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**Validation of Realistic 3D Computer Models of Ventricular Arrhythmias with Optical Mapping Experiments**

Flavio Fenton, PhD, Elizabeth M. Cherry, Isabelle Banville, Richard A. Gray, Harold M. Hastings, Alain Karma and Steven J. Evans. Beth Israel Medical Center, New York, NY, Hofstra University, Hempstead, NY, University of Alabama, Birmingham, AL and Northeastern University, Boston, MA.

We present the first quantitative comparison of computer simulations with experiments in full 3D mammalian ventricles. An anatomically correct rabbit ventricular model with fiber rotation was used along with an ionic cell model that reproduces the shape of the action potential (AP) as well as the restitutions of AP duration and conduction velocity measured experimentally using diacetyl monoxime (DAM) and cytochalasin D (CytoD). DAM simulations and experiments with isolated rabbit hearts using optical recordings both produced stable VT with an ECG spectral peak at  $135 \pm 5$  ms and  $140 \pm 10$  ms, respectively, characterized by a single stable spiral wave (Fig. A,B) with a linear core of length  $1 \pm 0.15$  cm and  $> 0.9$  cm, respectively. Simulations and experiments with CytoD yielded non-sustained VF characterized by multiple short-lived non-stationary reentrant waves (Fig. C). 3D analysis of numerical simulations showed that the complex dynamics using CytoD arose from an instability of the core induced by the anisotropic fiber rotation and dynamically created regions of dispersion of refractoriness produced by wave front-back interaction due to the large size of the wavelength relative to the ventricular size.

