496-109 High Resolution Imaging of Human Arterial Walls Via Optical Coherence Tomography

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Optical coherence tomography (OCT) is a recently developed technology which can perform micron scale, cross sectional tomographic imaging. OCT operates using interferometric optical ranging of low coherence infrared light or ultrashort laser pulses which are backscattered from tissue. This technique is analogous to the reflected acoustical wave measurements of conventional B mode ultrasound. In this study, two dimensional cross sectional images of in vivo human aorta and coronary artery sections obtained postmortem. The microstructure of normal and atherosclerotic tissue was displayed as a false color or grayscale image. The bandwidth of the photodetector source (1300 nm) allowed a resolution of 20 microns, almost 10 times greater than conventional intravascular ultrasound. Different morphologies including fatty, fibrous, and water based tissue, were well differentiated in the images and corresponded to histologic sections. Imaging was possible with up to 1 mm penetration into the tissue with little attenuation from heavy calcification. The typical image acquisition time was in the range of 2-3 seconds. A more detailed analysis of the optical properties of relatively uniform, structurally distinct tissues, such as adipose, skeletal muscle, and tendon, was performed to further confirm the contrast between fat, muscle, and connective tissue. The contrast ratios of muscle, tendon, and fat, were measured to be 1:78:22, respectively. The effective refractive indices and optical penetration depths in different tissue types were also measured. OCT is promising new technology for high resolution "optical biopsy". It does not require direct contact with the vessel wall and could be performed via a catheter integrated with a relatively inexpensive fiber optic bundle. Future studies utilizing currently available femtosecond lasers are expected to both increase the resolution of OCT which is dependent on bandwidth or pulse duration, to nm-4 microns and allow visualization of structures deeper into tissues.

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Tuesday, March 21, 1995, 9:00 a.m.-11:00 a.m. Ernest N. Morial Convention Center, Hall E Presentation Hour: 9:00 a.m.-10:00 a.m.

497-110 Measurement of Adenylyl Cyclase Activity in the AV Nodal Region of the Canine Heart: Evidence for Inhibition by Adenosine and Acetylcholine

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Although essential to cardiac conduction, little is known about the biochemistry underlying post-receptor adrenergic, cholinergic, and purinergic processes in the AV node. To study these mechanisms, we developed a highly sensitive fluorometric assay for cAMP and used it to characterize regional adenylyl cyclase activity (ACA) (pmol/min/mg of protein) in membrane preparations from freeze-dried 20 micron thick micro-dissected pieces of canine (n = 6) right atrium (RA), AV nodal region (AVN), and left ventricle (LV). Adjacent sections were stained for acetylcholinesterase activity to identify the AVN. Basal and NaF-stimulated ACAs (mean±SEM) were 7.2 ± 0.4 and 72.4 ± 0.5 in RA, 15.6 ± 1.3 and 58.8 ± 4.7 in AVN, and 6.8 ± 0.9 and 66.7 ± 5.0 in LV, respectively. Isoproterenol (10^-7 to 10^-5 M) increased ACA in a dose-dependent fashion and the increment of cAMP production rate was similar in three different regions. Adenosine (10^-3 M) and carbachol (10^-5 M) inhibited isoproterenol (10^-6 M)-stimulated ACA as follows:

Results of this study demonstrate for the first time that (1) there are significant regional differences in ACA under basal conditions and after adrenergic, purinergic, and cholinergic stimulation in the heart, and (2) adenosine inhibits ACA in the RA, AVN and LV, whereas the inhibitory effects of cholinergic stimulation are more specific for the AVN.

496-109 Measurement of Right Ventricular Mass of Small and Large Hearts by Quantitative Volume-Rendered Three-dimensional Echocardiography Without the Use of Geometric Assumptions: Experimental Validation

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Despite a need for a method to measure right ventricular (RV) mass, the unusual geometry of the RV has made application of common imaging approaches unreliable. Recent developments in volume-rendered three-dimensional echocardiography (3DE) suggest that this technique could not only depict the anatomy but also aid in quantitation. Previously we have shown the utility of 3DE in obtaining RV cavity volumes. In this study we explored the accuracy of volume-rendered 3DE in estimating RV mass. Using a rotational imaging approach with a 5 MHz transducer, we obtained 2D images of 15 animal (dogs/pigs/cows) hearts of various sizes (simulating pediatric and adult hearts) in a watertank at every 2 degrees over a 180 degree span. Using various steps of 3D image processing (digital reformatting, thresholding and segmentation), 3DE images of the hearts were developed. Electronically, we sectioned each heart into 30 equidistant parallel slices that were compared to the actual dry weight of the anatomic RV free wall measured by a third observer. Results: The actual RV mass of the anatomic hearts was (M ± SD) 72 ± 44 grams (range 25-175 grams); 3DE measured RV mass was 84 ± 55 grams (range 25-218 grams). 3DE (y) derived RV mass had an excelent correlation with actual mass (x) : y = 1.22 x - 5.4, r = 0.98, p < 0.0001. The interobserver concordance was also excellent (r = 0.97). In addition to such quantitative data, volume-rendered 3DE yielded tissue-depiction images of the RV interior, displaying the endocardial surface, papillary muscles and moderator band, and detailed visualization of the RV inflow and outflow regions in many cut-sections. 3DE projections also allowed visualization of the interventricular septum on end. We conclude that volume-rendered 3DE can be used to derive RV mass measurements accurately without unreliable geometric assumptions. This quantitative ability coupled to the capability of displaying RV anatomy enhances the clinical potential of 3D echocardiography.

497-111 β Blockade Selectively Eliminates Slow Antegrade Atrioventricular Nodal Conduction in the Rabbit

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We studied the effects of an β blocker, risotilide (R) on the dynamic properties of perfused rabbit AV nodes using intermittent right atrial premature pacing and bipolar surface electrograms. R was serially perfused with 1, 3 and 6 x 10^-6 M R for 15 minutes following pre-drug measurements.
Results: Typical changes in the antegrade recovery curve produced by R are shown in the figure. There was a concentration dependent decrease in ΔAH from the pre-drug value of 56 ± 15 ms to 29.2 ± 16.9 ms and 13.7 ± 5.9 ms by 3 and 6 x 10⁻⁶ M respectively (n = 6). A reciprocal increase in the AV node effective refractory period was observed from 91 ± 15 ms (pre-drug) to 139 ± 16 ms (3 x 10⁻³ M) and 170 ± 16 ms (6 x 10⁻³ M). AH was unchanged at any concentration of R.

Conclusions: These results suggest that class III antiarrhythmic agents may increase action potential duration and the refractory period of the structure(s) limiting AV conduction and thereby eliminate a majority of the "slow" AV node conduction. These findings may have important implications for a pharmacologic approach to the treatment of AV node reentry tachycardias.

Has the Inotropic Effect of the Class-III Antiarrhythmic Drug Amiodarone a Frequency-depending Effect in Vivo?

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The prolongation of the action potential duration (APD) by class-III antiarrhythmic drugs causes in vitro a positive inotropic effect. On the other side a frequency-dependency of the APD-prolongation ("reverse use-dependence") was described. This would mean, that a heart rate reduction should have a positive effect on myocardial contractility after administration of class-III drugs.

We examined the hemodynamic effects of amiodarone (10 mg/kg, 20 mg/kg and 100 mg/kg) in thoracotomized rats vs. saline controls (NaCI) without and with bradycardia. Heart rate reduction was produced by vagal stimulation (reduction about 50%). Besides measurements in the intact circulation isovolumic maximum registrations (isolov. LVSP, isolov. dp/dt max) were performed to determine myocardial contractility.

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<td>D-SOT 10⁻⁶ M</td>
<td>+2 ± 3</td>
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<td>+4 ± 2</td>
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<td>D-SOR 10⁻⁵ M</td>
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<td>D-SOT 5 x 10⁻⁵ M</td>
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<td>QUIN 10⁻⁶ M</td>
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<td>+22 ± 6</td>
<td>+18 ± 4</td>
<td>+28 ± 4</td>
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<tr>
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<tr>
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<td>+3 ± 2</td>
<td>+4 ± 2</td>
<td>-3 ± 2</td>
<td>+5 ± 3</td>
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Conclusions: Neither of the three drugs with class III-action shows a reduction of DSP. While QUIN and D-SOT show dose-dependent increase in DSP, especially at long CLs, AMIO tissue concentrations are not related to DSP and no increase is seen at long CLs. These effects on DSP may explain the different clinical incidence of torsade de pointes between the three drugs.