

Video Article

February 2012: This Month in JoVE

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Abstract

The February issue of the Journal of Visualized Experiments (JoVE) takes a clinical theme with the release of two articles, which demonstrate implantations of medical devices used to treat cardiac arrhythmia. More specifically, both articles focus on treating atrial fibrillation - a devastating condition that can ultimately lead to stroke.

The first procedure, led by Professor Dietmar Baensch from the University Hospital Rostock, involves the surgical implantation of an implantable cardioverter-defibrillator, or ICD. ICDs are devices widely used for the termination of ventricular arrhythmias. However, if the site of abnormal pacemaking is supraventricular in origin, such as in the left atrium, these devices can deliver inappropriate and painful shocks. To overcome this issue with potential misdiagnosis, as well as higher complication rates observed with dual chamber electrodes, Biotronik has developed a single ICD lead, which is capable of both atrial and ventricular sensing. Guided by X-ray fluoroscopy and electrophysiology, Dr. Baensch and his team demonstrate the surgical procedure for inserting, testing, and anchoring the single chamber electrode. Following electrode positioning, the Lumax defibrillator is joined to the electrode and inserted into the patient. To assess device function ventricular fibrillation is induced via a T-wave shock, and the ability of the defibrillator to sense arrhythmia and administer a corrective shock to is assessed.

While the Lumax ICD system can attenuate cardiac arrhythmia by correcting cardiac pacemaking, the WATCHMAN left atrial appendage (LAA) occlusion device from Boston Scientific is designed to address a severe complication with atrial fibrillation - thromboembolic stroke. In patients with atrial fibrillation, the left atrial appendage, a muscular pouch in the left atrium, can act as a reservoir for clotting blood, which if dislodged, can form emboli that can cause stroke. When implanted, the WATCHMAN device can trap clots within the LAA before they exit. Following assessment of LAA morphology, our authors, led by Dr. Sven Möbius-Winkler from the University of Leipzig, demonstrate methods for inserting a guidewire through the femoral artery into the heart, advancing the device into the left atrium, and deployment of the device in the left atrial appendage. Studies have shown that patients receiving WATCHMAN intervention have a reduced probability of adverse cardiac events when compared to patients given the anticoagulant medication warfarin.

While both the Lumax ICD system and the WATCHMAN occlusion device show promise for treating cardiac arrhythmia and its complications, neither device is approved for use in the US. Through video-publication in JoVE, our authors have provided a resource for US physicians to view these sensitive device implantation procedures before they become available across the Atlantic.

One consequence of thromboembolism is hypoxia, and JoVE travels to the University of Rochester to document a method for 2-photon imaging of microregional hypoxia in the cerebral cortex. Our authors illustrate a detailed open cranial window preparation followed by 2-photon imaging of endogenous nicotinamide adenine dinucleotide, or NADH, fluorescence. NADH is well known for its ability to transport electrons during cellular respiration, and it just so happens that NADH fluorescence exhibits a nonlinear relationship with the partial pressure of oxygen in tissues. In the cortex, NADH fluorescence increases as hypoxia is induced, allowing these investigators to determine which cortical areas are most vulnerable to hypoxia, as well as the geometrical pattern of oxygen diffusion from vessels.

For Bioengineering, JoVE heads to Wayne State University to capture a procedure for visualizing the breast cancer tumor microenvironment, *in vitro*. Our authors demonstrate a procedure for the assembly of a breast cancer co-culture system, which they refer to as **Mammary Architecture and Microenvironment Engineering**, or MAME. Briefly, these culture models consist of a layer of human breast fibroblasts in collagen 1 matrix, below a layer of reconstituted basement membrane matrix, upon which ductal carcinoma cells from the breast are added before the entire model is submerged in medium. When imaged in 4D, or in 3 dimensions over time, the proliferation of carcinoma cells can be tracked. In addition, degradation of the basement membrane can be assessed as well, thanks to the incorporation of a type of collagen that fluoresces when hydrolyzed. This innovative culture system can provide insight for breast cancer researchers into the proteolytic pathways that promote invasive phenotypes in breast cancer cells and can be used to screen for new small molecule inhibitors that may hinder tumor proliferation.

In Immunology and Infection, JoVE shifts its focus to vector borne disease, where investigators from the Center for Disease control in Fort Collins, Colorado, present three fundamentally important procedures for understanding how infectious pathogens migrate through the tick. The first procedure involves removing one of the legs from the tick, which enables the collection of hemolymph - the fluid carries oxygen to the tick's organs. The bacteria that cause Lyme Disease, *Borrelia burgdorferi*, will move to the hemolymph of the tick once a bloodmeal has been absorbed by the midgut. The second dissection protocol illustrates steps for accessing the hemocoel and removing the salivary glands, which is where *Borrelia* reside before transmission to a host. The final protocol begins with application of the muscarinic agonist, pilocarpine, to the dorsal surface of an engorged tick, in order to induce salivation. Saliva is collected from a mouthpart referred to as the hypostome and manual techniques for promoting tick salivation via gentle massage, are demonstrated.

From vector borne disease to medical device implantation, February is brimming with content submitted from authors dedicated to understanding and treating human disease. Other notable articles for the month of February include methods for assessing the metastatic potential of ovarian

cancer, spatial analysis of neuropeptides in a rodent model of Parkinson's, and measurements of ventricular pressure in neonatal and embryonic mice. From bench to bedside, no other journal provides a window into biomedical research quite like JoVE. Stay tuned for February's content!

Video Link

The video component of this article can be found at <https://www.jove.com/video/4258/>

Protocol

MALDI Imaging Mass Spectrometry of Neuropeptides in Parkinson's Disease

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Dopamine replacement pharmacotherapy using L-DOPA is the most commonly used symptomatic treatment of Parkinson's disease, but is accompanied by side effects including involuntary abnormal movements, termed dyskinesia¹. Here, a protocol for MALDI imaging mass spectrometry is presented that detects changes in rat brain neuropeptide levels related to dyskinesia.

Detection of Microregional Hypoxia in Mouse Cerebral Cortex by Two-photon Imaging of Endogenous NADH Fluorescence

Oksana Polesskaya¹, Anita Sun², Gheorghe Salahura², Jharon N. Silva¹, Stephen Dewhurst¹, Karl Kasischke³

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Here we describe a method to directly visualize microregional tissue hypoxia in the mouse cortex in vivo. It is based on concurrent two-photon imaging of nicotinamide adenine dinucleotide (NADH) and the cortical microcirculation. This method is useful for high resolution analysis of tissue oxygen supply.

MAME Models for 4D Live-cell Imaging of Tumor: Microenvironment Interactions that Impact Malignant Progression

Mansoureh Sameni¹, Arulselvi Anbalagan¹, Mary B. Olive¹, Kamiar Moin^{1,2}, Raymond R. Mattingly^{1,2}, Bonnie F. Sloane^{1,2}

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We have developed 3D coculture models for live-cell imaging in real-time of interactions among breast tumor cells and other cells in their microenvironment that impact progression to an invasive phenotype. These models can serve as preclinical screens for drugs to target paracrine-induced proteolytic, chemokine/cytokine and kinase pathways implicated in invasiveness.

The WATCHMAN Left Atrial Appendage Closure Device for Atrial Fibrillation

Sven Möbius-Winkler, Marcus Sandri, Norman Mangner, Phillip Lurz, Ingo Dähnert, Gerhard Schuler

University of Leipzig Heart Center

The accompanying video describes a procedure for percutaneous placement of the WATCHMAN Left Atrial Appendage (LAA) Device. The WATCHMAN is a nitinol device designed to be permanently implanted at, or slightly distal to, the opening of the left atrial appendage (LAA) to trap blood clots before they exit the LAA, preventing thromboembolic stroke.

Measuring Left Ventricular Pressure in Late Embryonic and Neonatal Mice

Victoria P. Le¹, Attila Kovacs², Jessica E. Wagenseil¹

¹Department of Biomedical Engineering, Saint Louis University, ²Department of Internal Medicine, Washington University School of Medicine

Measuring left ventricular pressure (LV) in embryonic and neonatal mice is described. Pressure is measured by inserting a needle connected to a fluid-filled transducer into the LV under ultrasound guidance. Care must be taken to maintain normal cardiac function during the experimental protocol.

In vitro Mesothelial Clearance Assay that Models the Early Steps of Ovarian Cancer Metastasis

Rachel A. Davidowitz, Marcin P. Iwanicki, Joan S. Brugge

Department of Cell Biology, Harvard Medical School

The mesothelial clearance assay described here takes advantage of fluorescently labeled cells and time-lapse video microscopy to visualize and quantitatively measure the interactions of ovarian cancer multicellular spheroids and mesothelial cell monolayers. This assay models the early steps of ovarian cancer metastasis.

Saliva, Salivary gland, and Hemolymph Collection from Ixodes Scapularis Ticks

Toni G. Patton¹, Gabrielle Dietrich², Kevin Brandt¹, Marc C. Dolan², Joseph Piesman², Robert D. Gilmore Jr.¹

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The collection of infected tick hemolymph, salivary glands, and saliva is important to study how tick-borne pathogens cause disease. In this protocol we demonstrate how to collect hemolymph and salivary glands from feeding *Ixodes scapularis* nymphs. We also demonstrate saliva collection from female *I. scapularis* adults.

A New Single Chamber Implantable Defibrillator with Atrial Sensing: A Practical Demonstration of Sensing and Ease of Implantation

Dietmar Bänsch, Ralph Schneider, Ibrahim Akin, Cristoph A. Nienaber
Heart Center Rostock, University Hospital of Rostock, Germany

Dual-chamber implantable cardioverter-defibrillators (ICDs) may improve detection of atrial fibrillation as well as differentiation of tachycardias. However, this advantage is undermined by complications associated with the second electrode, which is required in conventional dual chamber devices. Therefore, BIOTRONIK has developed a new electrode called the Linx^{SMART} S DX that, when used in conjunction with the Lumax DX ICD, offers dual-chamber detection without the risks associated with the second electrode.

Disclosures

No conflicts of interest declared.