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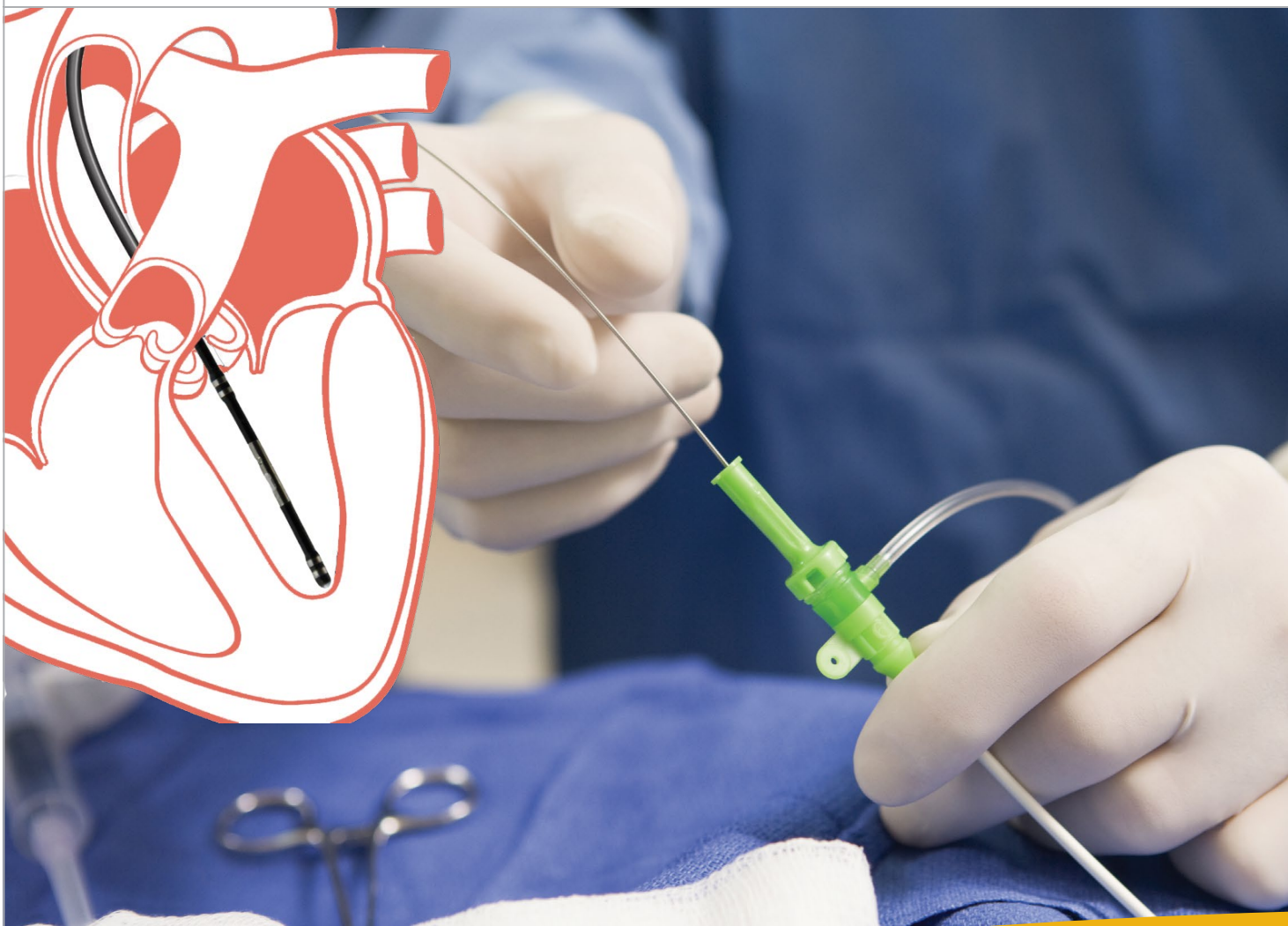
Surgical Protocols: An In-Depth Look



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Mouse Left Ventricle PV Measurement (Open Chest)

APPLICATION BASICS

Site:	Left Ventricle - Open Chest
Species:	Mouse
Body Weight:	20- 50 grams
Duration:	Acute

CATHETER

Size:	1.2F
Type:	Pressure Volume
Catalog #:	FTH-1212B-3518, FTH-1212B-4018, FTH-1212B-4518

SYSTEM

ADV500 / ADVantage

Application

The hemodynamic properties measured by the pressure-volume system can be used to determine cardiac function. Performing an IVC occlusion as part of the pressure-volume measurement process allows for the determination of load-independent indices.

Anatomical Landmarks

Open chest approach - thorax/upper abdomen area over the xyphoid, proximity of the sternal manubrium. Cut through the diaphragm to expose the apex of the heart. To reduce bleeding avoid incisions around the sternum.

Surgical Approach

Secure animal in supine position on the heating pad. Make skin incision in the lower thorax/ upper abdomen area over the xyphoid (Fig 1). Separate the skin from the chest wall by blunt lateral dissections. Open the abdominal wall in the proximity of the sternal manubrium (Fig 2). Use 45 cm 5-0 softsilk on 3/8 circle 19 mm cutting needle to penetrate xiphoid and to pull and attach 5-0 suture proximally (towards the mouse's head) (Fig 3). Cut through the diaphragm (Fig 4) to expose the heart apex (Fig 5). Try to avoid any incisions around sternum to limit bleeding. Try not to artificially retract rib cage. Gently maneuver the apex, using Q-tips into the diaphragm opening. Using microinstruments, bluntly open pericardium (Fig 6).

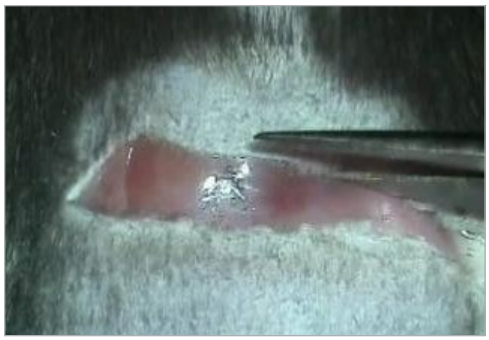

Fig. 1: Initial incision in the upper abdomen

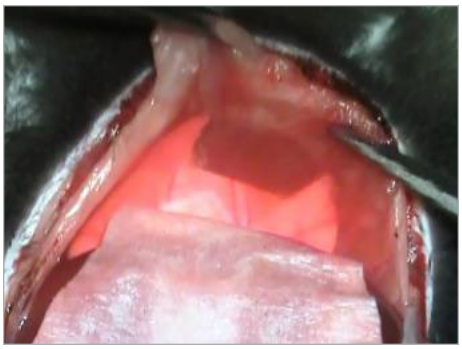

Fig. 2: Opening the abdomen wall

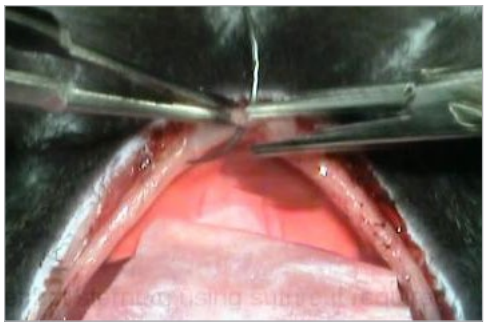

Fig. 3: Use a suture to hold the xiphoid in place

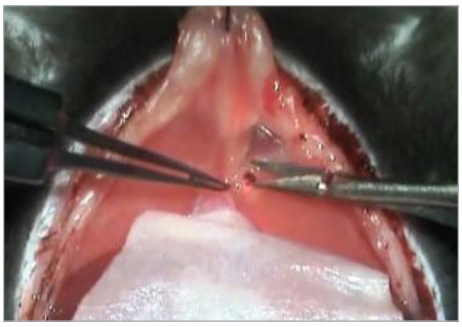

Fig. 4: Cut through the diaphragm

Use the 27 gauge needle for the LV apical stab (Fig 7). After successful stab, blood is found in the needle tip. As needle is withdrawn from the LV myocardium with your hand or with forceps covered by PE tubing, insert the 1.2F Catheter through the stab wound (Fig 8) until the distal electrode of the catheter is fully surrounded by

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Cardiovascular Division, British Heart Foundation Excellence Centre, King's College London, St Thomas' Hospital, London SE1 7EH, UK

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Mouse Left Ventricle PV Measurement (Open Chest) Cont.

Surgical Approach Cont.

LV muscle (Fig 9). This is a critical step, for all electrodes have to be fully submerged in the ventricle's cavity. Position the Catheter to control for phase angle (ɵ) and admittance magnitude (Y) and collect pressure-volume (PV) signal in the form of a PV loop tracing.

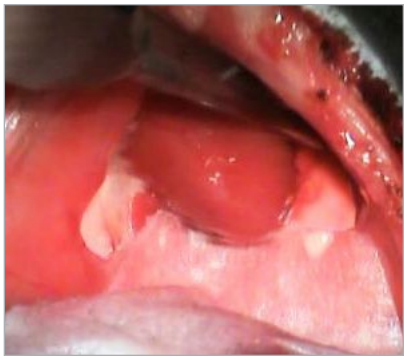

Fig. 5: Expose the heart apex

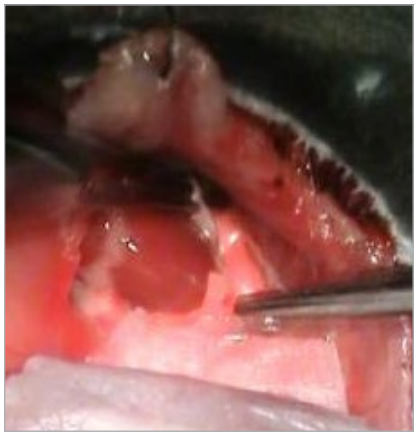

Fig. 6: Open the pericardium

Allow Catheter to stabilize in the LV for 5-10 min before marking the data file to start protocol. Catheter positional adjustment needs to be made based on acquired signals, mostly coming from phase angle (ɵ) and admittance magnitude (Y) recordings. Both signals should have a sinusoidal wave profile. If the PV Catheter lies in an off-center position, the phase signal may be distorted (signals will be relatively high with a low amplitude). Reposition the Catheter until a more central position is found, where magnitude waves are at their largest and phase waves are stable and devoid of noise or spikes. See "Proper PV Catheter Placement in the Left Ventricle" for more details. Once optimal Catheter position is obtained, perform a "baseline scan" on the ADV500/ADVantage control unit - end-systolic and end-diastolic blood conductance ($G_{b\text{-}ED}$ and $G_{b\text{-}ES}$) values will be sampled and reported on the LCD screen. This scan is best conducted when the ventilator is turned off a few seconds prior to scanning and for the duration of the scan. Repeat the baseline scan, as necessary, throughout the experiment to ensure most accurate report of volume. Record load-dependent values during steady state for at least 10 min for each animal before attempting IVC occlusion.

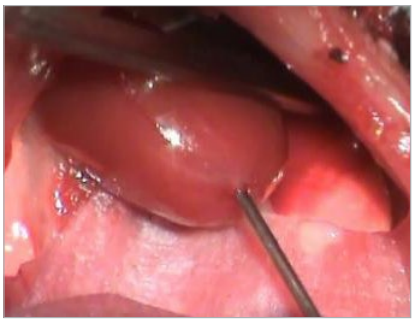

Fig. 7: Stab apex with 27G needle

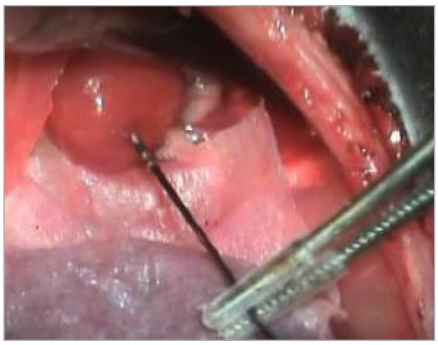

Fig. 8: Carefully insert Catheter into stab wound

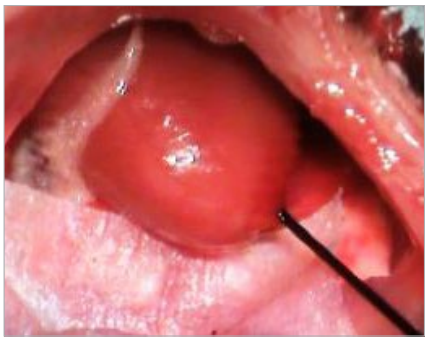

Fig. 9: Submerge all electrodes

IVC occlusion is used to derive various load-independent indices of cardiac function. Abdomen is opened and (5-0 silk) suture is placed under the vena cava, carefully separated from adventicia and thoracic aorta, above the liver at close proximity of the heart. This position will ensure an immediate drop of blood volume to better control and compare data sets. IVC occlusions can be performed by pulling on a suture placed around the vessel. Shut off the ventilation for a few seconds prior to and during occlusion to acquire data without lung motion artifacts.

At the end of the experiment, carefully remove the PV Catheter by gently pulling it back through the stab wound. Immediately, insert Catheter tip into 5 ml saline pre-filled syringe. Clean Catheter as soon as possible according to proper care guidelines to considerably prolong the Catheter's life, see "Cleaning Guidelines for Catheters."

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Mouse Left Ventricle PV Measurement (Closed Chest)

APPLICATION BASICS

Site:	Left Ventricle - Closed Chest
Species:	Mouse
Body Weight:	20- 50 grams
Duration:	Acute

CATHETER

Size:	1.2F
Type:	Pressure Volume
Catalog #:	FTH-1212B-3518, FTH-1212B-4018, FTH-1212B-4518

SYSTEM

ADV500 / ADVantage

Application

The hemodynamic properties measured by the pressure-volume system can be used to determine cardiac function. Performing an IVC occlusion as part of the pressure-volume measurement process allows for the determination of load-independent indices.

Note: Preforming an IVC occlusion will require a second incision in the abdomen of the mouse.

Anatomical Landmarks

Right Carotid Artery (RCA) passes cranially along the right side of the trachea near the larynx in the close proximity to the vago-sympathetic trunk. Major muscles (sternohyoid and strenomastoid) in the area have to be moved aside to allow ventral neck access.

Surgical Approach

For right common carotid artery (RCA) access, secure animal in supine position on the heating pad. Using sharp scissors, starting immediately below the chin, make a straight incision towards the transversal pectoral muscles. Make the incision as straight as possible while lifting the skin with thumb forceps (Fig 1). Keep the scissor tips up. Using blunt scissors or medium hemostats, blunt dissect any underlying glandular tissue from skin around the entire circumference of the wound (Fig 2). Minor bleeding can be stopped by Q-tips or by pre-made spear shaped nitrocellulose sponges. Keep area moist with warm sterile saline or PBS. Gently separate glands via blunt dissection to expose underlying muscular layer and use retractors to make trachea and ventral neck muscle visible (Fig 3).

Bluntly dissect along the longitudinal right central and adjacent muscular group (sternocleidomastoid, thyrohyoid, sternohyoid, omohyoid) and remember to avoid pressure on these muscles to maintain the mouse's ability to breath. Carefully separate the central muscle from parallel neck muscles and the diagonal thin muscular band (omohyoid) lying directly over the carotid vasculature. Retract skin and muscular tissues for visualization of the underlying carotid artery (Fig 4). Keep the tips of the instruments up and all tissues moist and warm. During subsequent methodical dissection and retraction of adjacent tissue and sheets, RCA can be detected next to vago-sympathetic trunk (a thin white sheath lying next to the RCA).

Continue blunt dissection to expose RCA to about 20 mm in length. Dissect alongside the RCA distally towards the head to expose RCA's bifurcation into branches. Ensure that section of the RCA is completely separated from all adjacent tissues to limit an unexpected bleeding during the retraction and/or clamping procedures. RCA must be fully separated from vascular fascia and the vagus nerve.

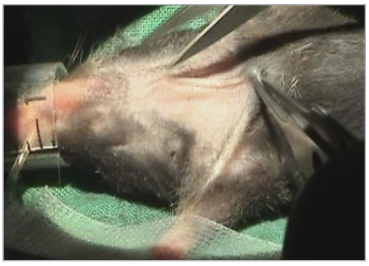

Fig. 1: Initial incision under the chin

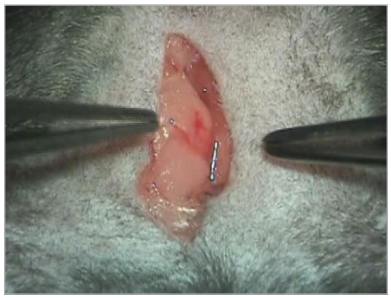

Fig. 2: Dissect glandular tissue from skin

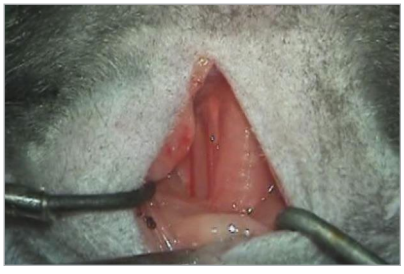

Fig. 3: Retract skin to expose site

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Mouse Left Ventricle PV Measurement (Closed Chest) Cont.

Surgical Approach Cont.

At this stage, 5-0 sutures can be placed around RCA to be used for retraction and/or clamping and hemostasis. Use micro-forceps to place sutures around the RCA (Fig 5). Place the first suture to the most proximal visible end on the RCA (as close to the head as possible) and tie it off using surgical knot (Fig 6), while creating tension with a clamp and retracting it towards the head. Place 2nd suture (Fig 7) and retract it distally towards the tail. At this point the RCA has been retracted proximally and distally and blood flow has been temporally stopped. Avoid excessive pressure on the vasculature and try to maintain normal vessel geometry. Slide 3rd suture under the segment but do not tie it off (Fig 7). This suture will be tied off when PV Catheter passes the second suture on the way into the aorta and heart. While creating tension on the distally placed sternal-suture, make a cut with micro-dissecting scissors closer to the head (proximally on the free RCA segment) (Fig 8). Keep in mind that a longer isolated section of the RCA will significantly improve chances for successful Catheter introduction.

Following a successful RCA arteriotomy, use a vascular introducer or micro forceps (Fig 9) to open and lift the incision, while exploring the size of this opening. Especially for a novice surgeon, who might require more time to successfully introduce the Catheter, an introducer might allow more time to locate the insertion site in the collapsed RCA, limiting blood loss on catheterization. When completely satisfied with the RCA opening, carefully proceed (Fig 10) and lift the sternal clamp and insert 1.2F tetrapolar pressure-volume Catheter into the opening by passing both sets of volume electrodes. Position and tie off the first suture around the Catheter past the second set of rings (Fig 11). At the same time, please make sure there is not an excessive resistance present upon introduction (vasoconstriction, vessel lumen distortion), which might cause excess bleeding out of the arteriotomy incision on repositioning(s).

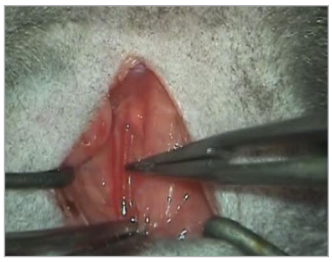

Fig. 4: Expose & dissect RCA

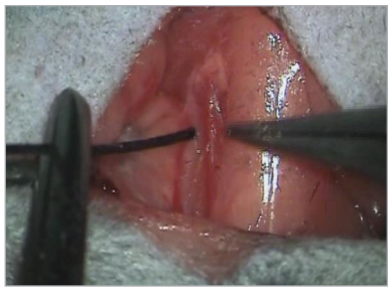

Fig. 5: Use hemostat to draw suture under the RCA

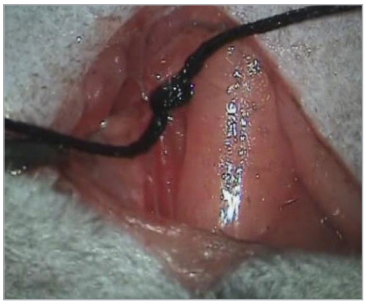

Fig. 6: Tie suture to proximal end of RCA

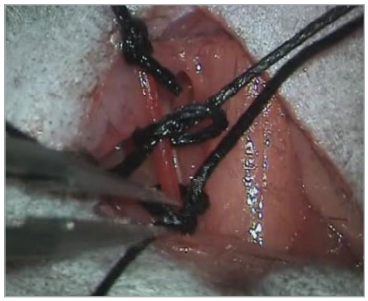

Fig. 7: Three sutures around the RCA

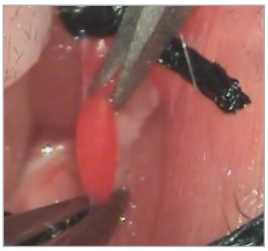

Fig. 8: Carefully cut RCA

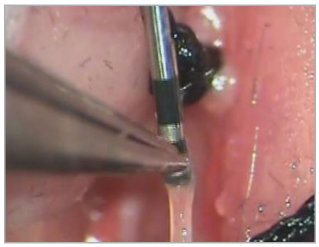

Fig. 9: Carefully insert Catheter

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Mouse Left Ventricle PV Measurement (Closed Chest) Cont.

Surgical Approach Cont.

With the Catheter in the RCA, get a feel for the degree of resistance by gently rotating the Catheter in the RCA. Slide the Catheter slowly towards the heart. Then tie off the second 5-0 suture around the Catheter to prevent it slipping out (Fig 12). Be careful not to damage the Catheter with the forceps tips, and be sure to hold the Catheter in the same plane as the blood vessel during the entire introduction process; please see "Optimizing Catheter Life Span." Position the Catheter to control for phase angle (ɵ) and admittance magnitude (Y) and collect pressure-volume (PV) signal.

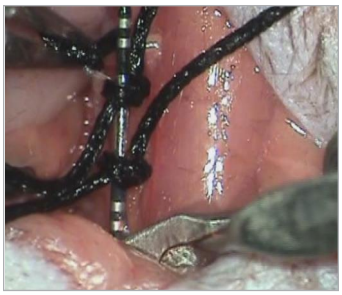


Fig. 10: Proceed with Catheter insertion

Allow Catheter to stabilize in the LV for 5-10 min before marking the data file to start protocol. Catheter positional adjustment needs to be made based on acquired signals, mostly coming from phase angle (ɵ) and admittance magnitude (Y) recordings. Both signals should have a sinusoidal wave profile. If the PV Catheter lies in an off-center position the phase signal may be distorted (signals will be relatively high with a low amplitude). See "Proper PV Catheter Placement in the Left Ventricle" for more details. Reposition the Catheter until a more central position is found, where magnitude waves are at their greatest and phase waves are stable and devoid of noise or spikes. Once the optimal Catheter position is obtained, preform a "baseline scan" on the ADV500/ADVantage control unit. End-systolic and end-diastolic blood conductance ($G_{b\text{-}ED}$ and $G_{b\text{-}ES}$) values will be sampled and reported on the LCD screen. This scan is best conducted when the ventilator is turned off a few seconds prior to scanning and for the duration of the scan. Repeat the baseline scan as necessary throughout the experiment to ensure the most accurate report of volume. Record load-dependent values during steady state for at least 10 min for each animal before attempting IVC occlusion.

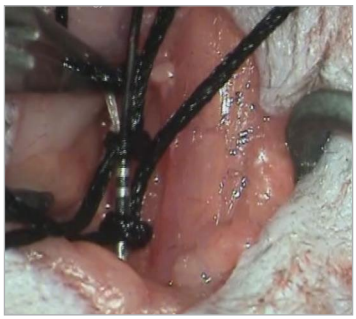


Fig. 11: Fully insert both sets of volume rings past the sutures

IVC OCCLUSION

IVC occlusion is used to derive various load-independent indices of cardiac function. In order to preform an IVC occlusion, a second surgical incision must be made in the abdomen to expose the vena cava. Carefully separate the vena cava from adventicia and thoracic aorta, above the liver close to the heart. The best technique is to place a 5-0 silk suture around the vena cava located as close as possible to heart. This position will ensure an immediate drop of blood volume to better control and compare data sets. IVC occlusions can be performed by pulling on a suture placed around the vessel. Shut off the ventilation for a few seconds prior to and during occlusion to acquire data without lung motion artifacts.

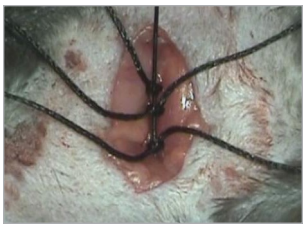


Fig. 12: Secure Catheter in place

At the end of the experiment, carefully remove the PV Catheter by gently pulling it back through the RCA. Immediately, insert Catheter tip into 5 ml saline pre-filled syringe. Clean Catheter as soon as possible according to proper care guidelines to considerably prolong the Catheter's life, see "Cleaning Guidelines for Catheters."

Rat Left Ventricle PV Measurement (Open Chest)

APPLICATION BASICS

Site:	Left Ventricle - Open Chest
Species:	Rat
Body Weight:	200 - 500 grams
Duration:	Acute

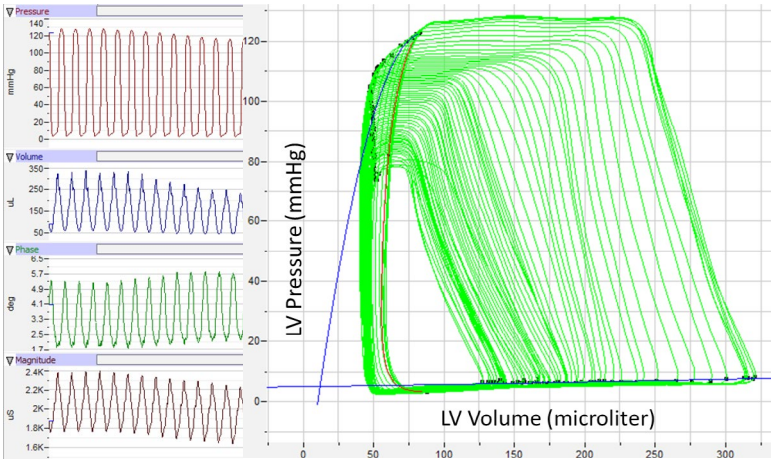
CATHETER

Size:	1.9F
Type:	Pressure Volume or VSL Pressure Volume
Catalog #:	FTH-1912B or FTH-1918B

SYSTEM

ADV500 / ADVantage

PV DATA AND LOOPS



Application

The hemodynamic properties measured by the pressure-volume system can be used to determine cardiac function. Performing an IVC occlusion as part of the pressure-volume measurement process allows for the determination of load-independent indices.

Surgical Approach

Prior to surgery, soak the tip of the PV Catheter in 0.9% saline for ~ 20 minutes. After soaking, adjust the pressure balance to zero for atmospheric pressure. See "Balancing Pressure Sensors Before Use" for guidelines.

Anesthetize rats with 3- 4% Isoflurane and maintain anesthesia with 2% Isoflurane by ventilator. Secure animal in dorsal position on the heating pad. Make V shape skin incision in the lower thorax/ upper abdomen area over the xyphoid (Fig. 1). Separate the skin from the chest wall by blunt lateral dissections. Open the abdominal wall in the proximity of the sternal manubrium (Fig. 2). Cut through the diaphragm to expose the heart apex (Fig. 3). Try to avoid any incisions around sternum to limit bleeding. Try not to artificially retract rib cage. Gently maneuver the apex, using Q-tips into the diaphragm opening.

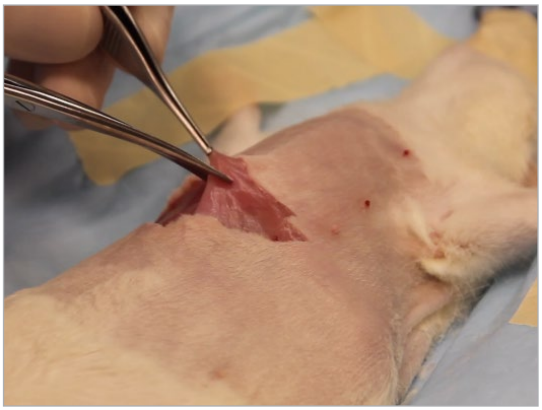


Fig. 1: Initial incision in the upper abdomen of rat in dorsal position

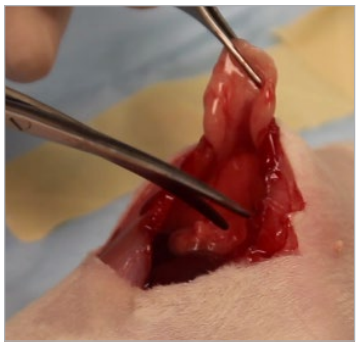


Fig. 2: Open the abdominal wall

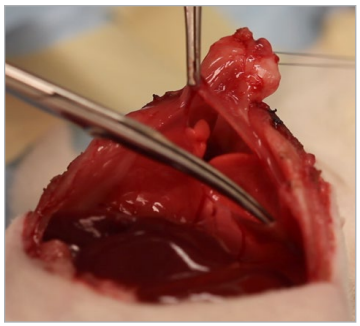


Fig. 3: Cut through the diaphragm to expose the heart apex

ACKNOWLEDGMENTS

Toronto General Research Institute, McEwen Centre for Regenerative Medicine, University of Toronto, 200 Elizabeth Street, MaRS 3-908, Toronto, ON, M5G 2C4, Canada.

REFERENCES

Konecny, F., Zou, J., et. al. "Post-myocardial infarct p27 fusion protein intravenous delivery averts adverse remodelling and improves heart function and survival in rodents." Cardiovasc Res 2012. 94, 492-500

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Rat Left Ventricle PV Measurement (Open Chest) Cont.

Surgical Approach Cont.

Use the 25G needle for the LV apical stab. After a successful stab, blood is found in the needle tip (Fig. 4). As the needle is withdrawn from the LV myocardium, with your other hand, insert the 1.9F Catheter through the stab wound (Fig. 5) until the distal electrode of the catheter is fully surrounded by LV muscle (Fig. 6). This is a critical step where all electrodes have to be fully submerged in the ventricle's cavity. Position the catheter to control for phase angle (ɵ) and admittance magnitude (Y) and collect pressure-volume (PV) signal.

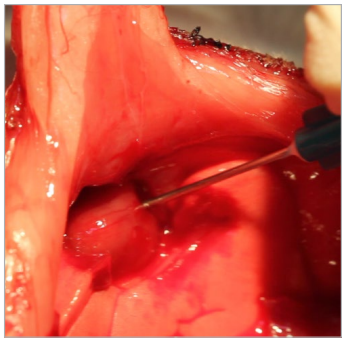

Fig. 4: Stab apex with a 25G needle

Allow the Catheter to stabilize in the LV for 5-10 min before marking the data file to start protocol. Catheter positional adjustment needs to be made based on acquired signals, mostly coming from phase angle (ɵ) and admittance magnitude (Y) recordings. Both signals should measure sinusoid wave signal. In the case of an off-center position, acquired sinusoid signals might be distorted as e.g. (low amplitude, frequency etc.). See "Proper PV Catheter Placement in the Left Ventricle" for more details. Reposition the Catheter until an optimal position is found – essentially this is where magnitude waves are at their largest and phase waves are stable and devoid of noise or spikes. The researcher should also view Pressure and Magnitude in an XY plane to assist in their search for optimal Catheter position. Once optimal Catheter position is obtained, perform a "baseline scan" on the ADV500/ADVantage control unit - end-systolic and end-diastolic blood conductance ($G_{b\text{-}ED}$ and $G_{b\text{-}ES}$) values will be sampled and reported on the LCD screen. This scan is best conducted when the ventilator is turned off a few seconds prior to scanning and for the duration of the scan. Repeat the baseline scan as necessary throughout the experiment to ensure the most accurate report of volume. Record load-dependent values during steady state for at least 10 min for each animal before attempting IVC occlusion.

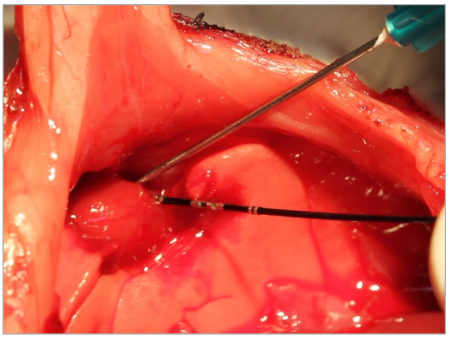

Fig. 5: Insert Catheter into the stab wound.

IVC occlusion is used to derive various load-independent indices of systolic function. During preparation of the open chest, an IVC occlusion suture (5-0 silk) is placed under the vena cava as it is carefully separated from its adventicia and thoracic aorta (Fig. 7). 5-0 silk is placed above the liver at close proximity of the heart. This position will ensure an immediate volume drop to better control and compare the data sets. IVC occlusions can be performed by pulling on a suture placed around the vessel (Fig. 8). Shut off the ventilation for a few seconds to acquire data without lung motion artifacts.

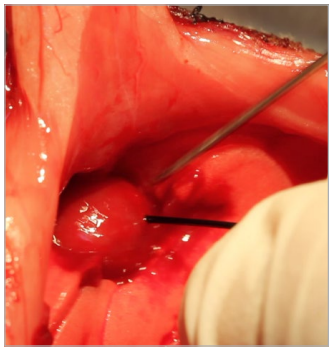

Fig. 6: Submerge all electrodes

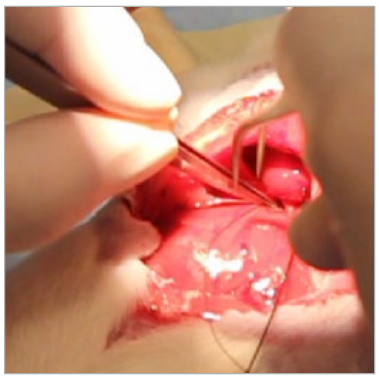

Fig. 7: Place sutures for IVC occlusion

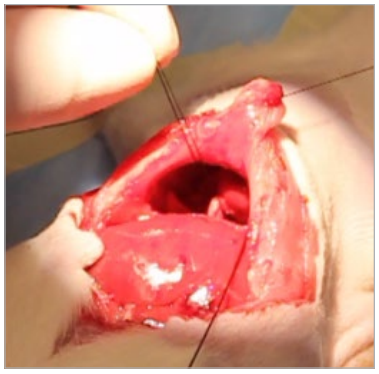

Fig. 8: Pull sutures to perform IVC occlusion

At the end of the experiment, carefully remove the PV Catheter by gently pulling it back through the stab wound. Immediately, insert Catheter tip into 5 ml saline pre-filled syringe. Clean Catheter as soon as possible according to proper care guidelines to considerably prolong the Catheter's life see "Cleaning Guidelines for Catheters."

Rat Left Ventricle PV Measurement (Closed Chest)

APPLICATION BASICS

Site:	Left Ventricle - Closed Chest
Species:	Rat
Body Weight:	200 - 500 grams
Duration:	Acute

CATHETER

Size:	1.9F
Type:	Pressure Volume or VSL Pressure Volume
Catalog #:	FTH-1912B or FTH-1918B

SYSTEM

ADV500 / ADVantage

Application

The hemodynamic properties measured by the pressure-volume system can be used to determine cardiac function. Performing an IVC occlusion as part of the pressure-volume measurement process allows for the determination of load-independent indices.

Note: Performing an IVC occlusion will require a second incision in the abdomen of the rat.

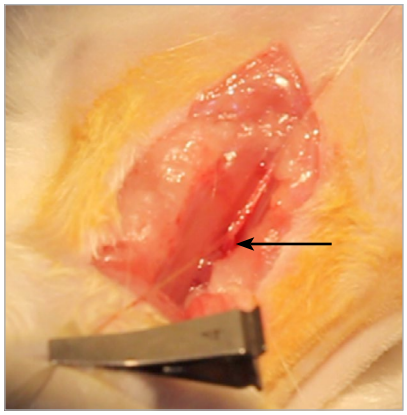

Fig. 1: Isolated RCA with sutures knotted around artery

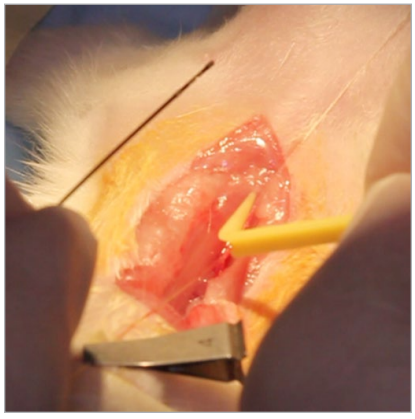

Fig. 2: Vascular introducer (yellow) is used to open the RCA in preparation for Catheter insertion

Surgical Approach

For right common carotid artery (RCA) access, secure animal in supine position on the heating pad. Using sharp scissors, starting immediately below the chin of the animal, make a straight incision in the direction towards the transversal pectoral muscles. Make the incision as straight as possible while lifting the skin with thumb forceps. Keep the scissor tips up. Using blunt scissors or medium hemostats, dissect any underlying glandular tissue from skin around the entire circumference of the wound. Take care to avoid major bleeding in the area. Minor bleeding can be stopped by Q-tip or gauze squares. Keep area moist with warm saline or PBS. Following this step, the skin should be completely separated from underlying tissues all the way around the incision. Using medium scissors, cut as straight as possible through the fascia overlying the glandular tissue to expose underlying glands. Gently separate glands via blunt dissection to expose underlying muscular layer.

Bluntly dissect along the longitudinal right central and adjacent muscular group (sternocleidomastoid, thyrohyoid, sternohyoid, omohyoid). Remember to avoid pressure on these muscles to allow the rat to breath. Carefully separate the central muscle from parallel neck muscles and the diagonal thin muscular band (omohyoid) lying directly over the carotid vasculature. Retract skin and muscular tissues for visualization of the underlying carotid artery vasculature. Keep the tips of the instruments up and all tissues moist and warm. During subsequent methodical dissection and retraction of adjacent tissue, RCA can be detected next to vago-sympathatic trunk (a thin white sheath lying next to the RCA).

Continue blunt dissection to expose RCA to about 25 mm in length. Dissect alongside the RCA distally towards the head to expose RCA's bifurcations. Ensure that section of the RCA is completely separated from all adjacent tissues to limit unexpected bleeding during the retraction and/or clamping procedures. RCA must be fully separated from vascular fascia and the vagus nerve.

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Rat Left Ventricle PV Measurement (Closed Chest) Cont.

Surgical Approach Cont.

At this stage, 5-0 sutures can be placed around the RCA to be used for retraction and/or clamping and hemostasis. Use micro-forceps to place sutures around the RCA. Place the first suture as close to the sternum as possible and then place a hemostat at the end to create tension towards the tail (Fig. 1). Place another suture around the RCA and double-knot tie this suture while creating tension with a clamp. Retract it towards the head (Fig. 1). At this point, the RCA has been retracted proximally and distally. The RCA's blood flow has been temporarily stopped. Note: Avoid excessive pressure on the vasculature and try to maintain normal vessel geometry. While creating tension on the sternal-suture, make a cut with micro-dissecting scissors in the middle of the free RCA segment. Keep in mind, a longer isolated section of the RCA will significantly improve chances for successful Catheter introduction. Next, loosely place a third 5-0 suture around the RCA and slide it towards the sternum. This suture will be tied off when the Catheter passes the first suture on the way into the aorta and heart.

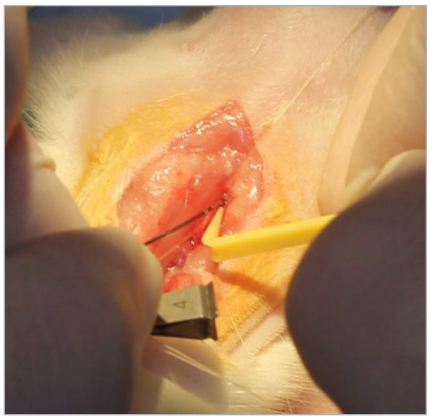

Fig. 3: Carefully remove the introducer and insert the Catheter

Following a successful RCA arteriotomy, use a vascular introducer to assist in opening and lifting vascular incision, while exploring the size of this opening (Fig 2). Note: Especially for a novice surgeon, who might take more time to successfully introduce the Catheter, the introducer might allow more time for the insertion in the collapsed RCA, limiting blood loss on subsequent attempted catheterizations.

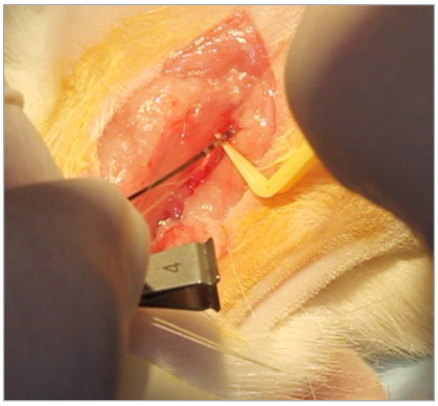

Fig. 4: Use the introducer to help Catheter insertion

When completely satisfied with the RCA opening, carefully proceed to insert the tetrapolar pressure-volume micro-manometer Catheter (Fig 3). Be careful not to damage the Catheter with the forceps tips and hold the Catheter in the same plane as the blood vessel during whole introduction (Please see "Optimizing Catheter Life Span" for best practices). Use the introducer's beveled tip to lift and level the Catheter to the same plane as the sternal RCA opening for a faster and smoother introduction into the first portion of RCA (Fig 4). Make sure there is not excessive resistance present on introduction (vasoconstriction, vessel lumen distortion), which might cause excess bleeding out of the arteriotomy site upon repositioning. Position the Catheter and tie off the first suture around the Catheter past the second set of rings. Ideally, there should be little bleeding. With the Catheter in the RCA, get a feel for the degree of resistance while gently rotating the Catheter in the RCA. Then tie off the third 5-0 suture around the Catheter to prevent it slipping out. Slide the Catheter slowly towards the heart. Position the Catheter to control for phase angle (ɵ) and admittance magnitude (Y). Both signals should measure sinusoid wave signal. In case of off-center position, acquired sinusoid signals might be distorted (low amplitude, frequency etc.). See "Proper PV Catheter Placement in the Left Ventricle" for more information.

Allow Catheter to stabilize in the LV for 5-10 min before starting the protocol. Once optimal Catheter position is obtained, preform a "baseline scan" on the ADV500/ADVantage control unit - end-systolic and end-diastolic blood conductance ($G_{b\text{-}ED}$ and $G_{b\text{-}ES}$) values will be sampled and reported on the LCD screen. This scan is best conducted when the ventilator is turned off a few seconds prior to scanning and for the duration of the scan. Repeat the baseline scan as necessary throughout the experiment to ensure most accurate report of volume. Record load-dependent values during steady state for at least 10 min for each animal before attempting IVC occlusion. Every time an adjustment is performed (Catheter position, ventilation, temperature etc.) re-record baseline PV.

Rat Left Ventricle PV Measurement (Closed Chest) Cont.

IVC OCCLUSION

IVC occlusion is used to derive various load-independent indices of cardiac function. In order to perform an IVC occlusion, a second surgical incision must be made in the abdomen to expose the vena cava. Carefully separate the vena cava from its adventicia and thoracic aorta, above the liver close to the heart. The best technique is to place a 5-0 silk suture around the vena cava as close as possible to heart. This position will ensure an immediate volume drop to better control and compare the data sets. IVC occlusion is performed by pulling upward on 5-0 suture. Shut off the ventilation for a few seconds prior to and during occlusion to acquire data without lung motion artifacts.

At the end of the experiment, carefully remove the PV Catheter by gently pulling it back through the RCA. Immediately, insert Catheter tip into 5 ml saline pre-filled syringe. Clean Catheter as soon as possible according to proper care guidelines to prolong the Catheter's life, see "Cleaning Guidelines for Catheters."

ACKNOWLEDGMENTS

Toronto General Research Institute, McEwen Centre for Regenerative Medicine, University of Toronto, 200 Elizabeth Street, MaRS 3-908, Toronto, ON, M5G 2C4, Canada.

REFERENCE

Konecny, F., Zou, J., et. al. "Post-myocardial infarct p27 fusion protein intravenous delivery averts adverse remodelling and improves heart function and survival in rodents." Cardiovasc Res 2012. 94, 492-500.

Rat Intracranial Pressure (ICP) Measurement

APPLICATION BASICS

Site:	Intracranial space (3 mm into parenchyma)
Species:	Rat
Body Weight:	400 - 650 grams
Duration:	Acute

CATHETER

Size:	1.6F
Type:	Pressure
Catalog #:	FTH-1611B-0018

SYSTEM

SP200, SP430, ADV500

Application

The measurement of Intracranial pressure (ICP) is an invasive procedure to determine the pressure inside the cranium. The cranium limits expansion capabilities of the brain; therefore, as volume increases in the cranium the ICP will also increase. Precise monitoring of pressure within the cranium can be valuable for a variety of applications, such as:

- Stroke
- Tumors
- Subarachnoid hemorrhage
- Severe brain injury
- Coma of unknown etiology
- Reye syndrome
- Hydrocephalus

Studies suggest improved clinical assessment from ICP waveform analysis. Specifically, ICP pulse pressure, measured by an invasive solid-state pressure micro-manometer, offers improved outcome when ICP waveforms are used as a treatment management target.

Surgical Approach

FEMORAL ARTERY CATHETERIZATION

Once stable surgical anaesthesia is confirmed, secure animal in dorsal position (supine) on the heating pad. Make a longitudinal skin incision in the inguinal area, approximately 15 mm in length, parallel to the linea alba (Fig 1). Use blunt dissection to separate connective tissue (cotton swabs, hemostats, scissors-blunt tip). Retract the incision to fully view the incision area (Femoral artery, vein and nerve).

Using fine tip forceps and cotton swabs, separate the femoral artery from the femoral vein. Separation is best performed when a perpendicular approach is used, as this will help avoid vascular tearing.

When bleeding occurs, a sterile cotton swab and/or gauze square should be placed on the segment and pressure should be applied on the area until bleeding ceases. Then continue with the surgery.

Place 2 pieces of 4.0 silk suture under the artery individually, such that the first thread lies distally towards the leg, while the second thread lies towards the body. Tie a loose knot on the side close to the body and place a hemostat in a direction that it creates a tension on the vessel temporarily obstructing the blood flow into the leg. Tie off the distal end suture (triple surgical knot) as far as possible and pull on the silk as far as possible to straighten the vascular access for more direct catheter placement.

Using the micro-dissecting scissors, make a small incision in the femoral artery at a 45 degree angle. Use a small vascular introducer to help insert the 1.6F Pressure Catheter.

Note: Refer to “Optimizing Catheter Life Span” for suggested Catheter handling techniques.

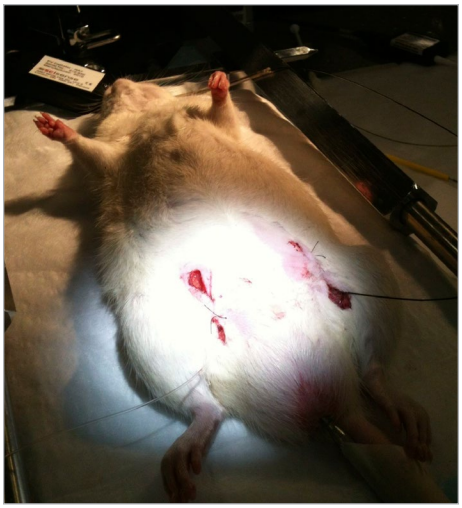

Fig. 1: Femoral artery catheterization

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Rat Intracranial Pressure (ICP) Measurement Cont.

Surgical Approach Cont.

Insert the Catheter into the vessel through the incision point (straightening the vessel to create tension often aids with insertion). After the Catheter is fully inserted into the femoral artery (approx. 6-7 cm), carefully tighten the anterior ligature around the artery.

Tip: Try to mark the 6-7 cm insertion point on the Catheter before inserting

Record the aortic pressure pulse. The abdominal aortic pressure waveform can be recorded as seen in Figure 5.

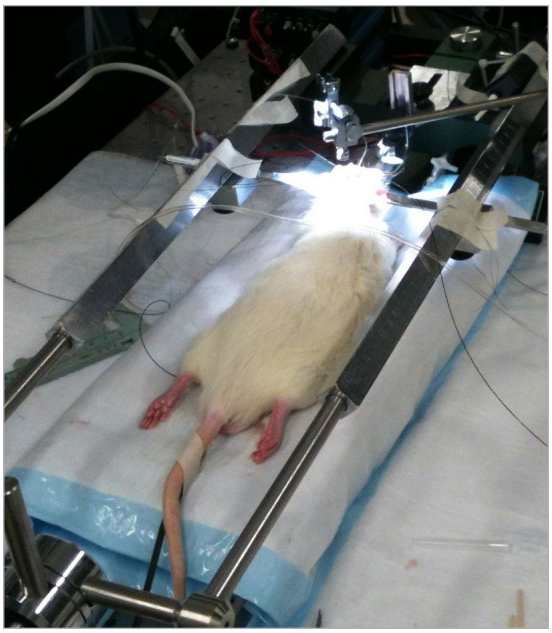

Fig. 2: Rat in stereotaxis apparatus for intracranial surgery

INTRACRANIAL SPACE CATHETERIZATION

After removing the hair from the rat's scalp, follow pre-op techniques as previously described.

Place the rat onto a stereotaxic apparatus by introducing the ear bars into the ear canal while tightening it into place. Make sure that the head is level with a ruler and check for a 90° angle between the ruler and the middle of the animal's scalp. Once level, lock the mouth with the anterior mount of the stereotaxic frame (Fig 2).

Next, a midline sagittal scalp incision is made to expose the Bregma and Lambda (Fig 3). If necessary, use cotton swabs to dry the exposed skull. The stereotaxic coordinates for intra-parenchymal intracranial pressure monitoring should be used.

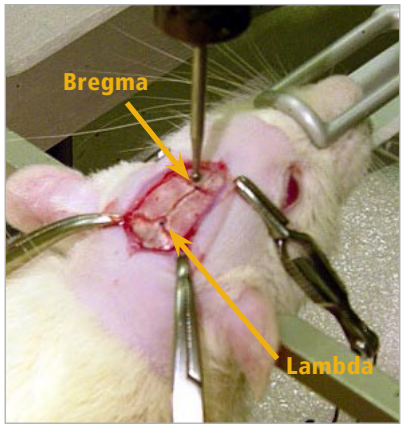

Fig. 3: Incision site for ICP catheterization

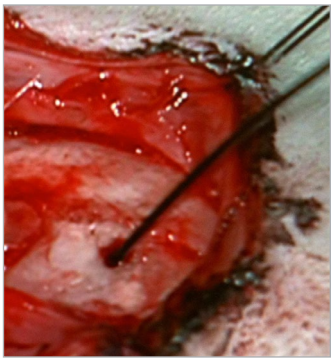

Fig. 4: Inserting Catheter into the parietal parenchymal.

The parietal coordinates for the intraparenchymal catheter placement is located 6 mm posterior to the Bregma and 2.5 mm lateral to the midline (Fig 4). Use an Archimedes micro hand drill to fashion a 0.7 mm burr hole over the coordinate. Note: care has to be taken to avoid plunging of the drill bit. Sharply incise the underlying dura mater using the bevel of a 23 gauge needle. The 1.6F Scisense Pressure Catheter is advanced through the burr hole into the brain parenchyma to a depth of 3 mm below the inner table of the parietal bone

At the end of the experiment, carefully remove both Catheters by gently puling it back from the burr hole and from femoral artery (cut the proximal surgical knot before retreating the Pressure Catheter). Immediately, insert the tip of the Catheters into 5 ml syringes filled with saline. Clean Catheters as soon as possible according to proper care guidelines to considerably prolong the Catheter's life see "Cleaning Guidelines for Catheters."

Rat Intracranial Pressure (ICP) Measurement Cont.

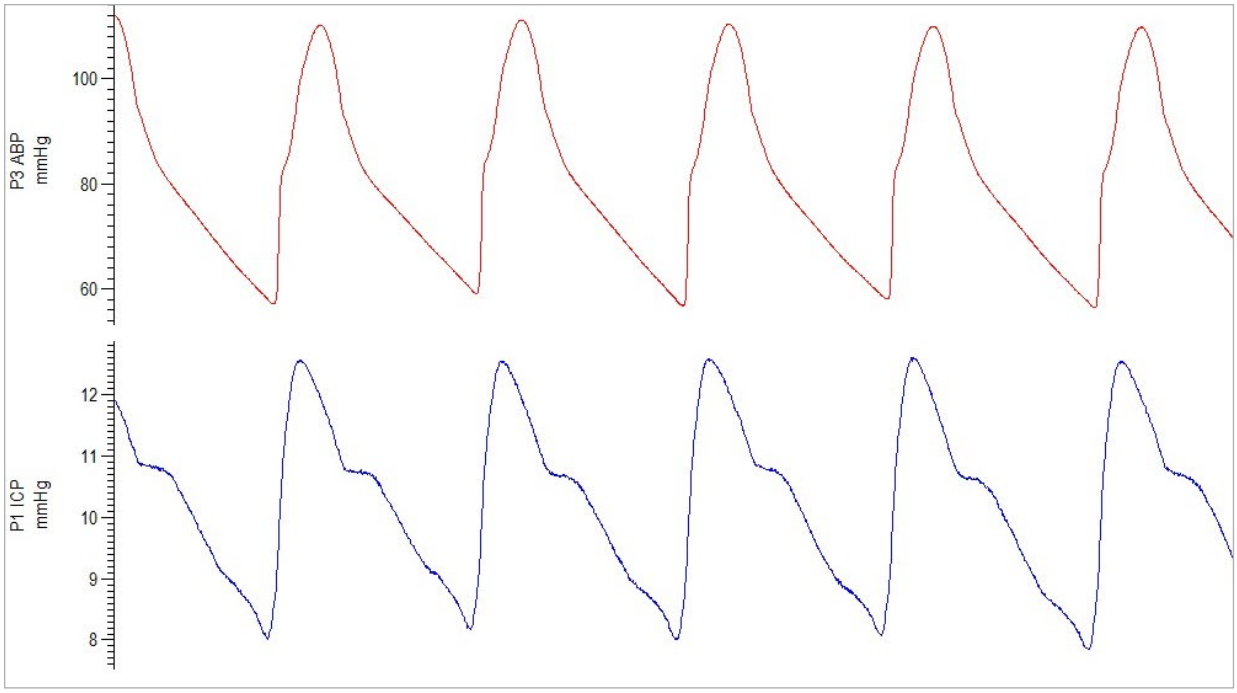

Fig. 5: Representative pressure wave tracings of ABP (arterial blood pressure) in the left femoral artery (red waveform) and Intracranial Pressure (ICP) (blue waveform), obtained by a micro pressure catheter introduced through a burr hole 3 cm below parietal bone.

ACKNOWLEDGMENTS

The animal research protocol used in this study was approved by Macquarie University's animal ethics committee. Methodology, pictures, and supporting data: courtesy of Dr Jonathan Li, Prof Stuart Graham and Prof. Alberto Avolio.

Measurement of Intracranial Pressure (ICP) in Rats© Courtesy of Dr Jonathan Li, Prof Stuart Graham and Prof. Alberto Avolio. The Australian School of Advanced Medicine, 2 Technology Place, Macquarie University NSW 2109, Australia.

REFERENCE

Kim MO, Li J, Qasem A, Graham SL, Avolio AP. "Frequency dependent transmission characteristics between arterial blood pressure and intracranial pressure in rats." Conf Proc IEEE Eng Med Biol Soc. 2012; 2012:5614-7.

Pig Left Ventricle PV Measurement (Closed Chest)

APPLICATION BASICS

Site:	Left Ventricle - Closed Chest, Right Femoral Artery or Right Carotid Artery Access
Species:	Pig (mini pig)
Body Weight:	20 - 70 kg
Duration:	Acute

CATHETER

Size:	5.0F or 7.0F
Type:	VSL Pressure Volume
Catalog #:	FDH-5018B-E(1, 2, 3 or 4)45(A or D) FDH-7018B-E(2, 3 or 4)45(A or D)

SYSTEM

ADV500 / ADVantage

Application

The hemodynamic properties measured by the pressure-volume system can be used to determine cardiac function. Performing an IVC occlusion (balloon catheter occlusion) as part of the pressure-volume measurement process allows for the determination of load-independent indices.

Anatomical Landmarks

Right femoral artery (RFA) is approached while the pig is placed in dorsal recumbence and the right rear leg is retracted laterally. RFA is located by palpating the area of inner thigh and pressure is applied to detect pulsation of the artery in the femoral canal.

The right carotid artery (RCA) passes cranially along the right side of the trachea near the larynx in the close proximity of vago-sympathetic trunk. In pigs, the RCA is located deeper, as compared to humans, which doesn't allow palpation of the arterial pulse. Major muscles (sternohyoid and sternomastoid) in the area might be moved aside to allow better ventral neck access. The RCA divides into: right external carotid artery to supply head and neck and the right internal carotid artery that passes through carotid canal into base of skull.

ENDOTRACHEAL (ET) INTUBATION

Endotracheal intubation ensures artificial control of respiration and protects the airways from aspiration of foreign material. When anesthetizing pigs for more than 1 hour, ET intubation is recommended. ET intubation is typically performed orotracheally after 10-15 min of gaseous anesthesia. Prepare Laryngoscope with long straight handle (250 mm), local anesthetic spray (Xylocaine endotracheal spray, 2% Lidocaine), syringe with air, tape for tracheotube (TT) fixation and slings to open the mouth. Allow the pig's head to be situated close to the end of the surgical table. V shaped stainless steel surgical table is one of best for head stabilization. Constantly aspirate saliva to limit salivation and use Atopine or Glycopyrrolate.

To introduce tracheotube (TT), open the mouth wide using slings and pull the tongue out. Introduce the laryngoscope to the vocal chords and spray both chords with Lidocaine. Withdraw the laryngoscope and about 5 min later re-introduce both the laryngoscope and tracheotube, pre-sprayed with xylocaine. The laryngoscope is passed into the pharyngeal cavity and depresses the tongue, exposing the epiglottis. The tip of the laryngoscope is then used to press the epiglottis upward towards the base of the tongue, revealing the laryngeal opening. Introduce TT into larynx through the vocal cords. TT is then advanced into the trachea during expiration. The pig will cough reflexively when TT is inserted, and might expel a large amount of air through TT. Inflate the balloon cuff with air, and connect TT to the anesthesia machine. TT is then fixed on the snout and taped. Any signs of cyanosis or gasping may indicate improper TT placement. If possible, shorten the anesthesia circuitry to limit dead space.

Insufficient anesthesia and unsuccessful repeats to insert TT may lead to laryngospasm. Resistance should not be felt on insertion. If you feel resistance on TT introduction, please remember that pigs have a right cranial bronchus located before the tracheal bifurcation and also some breeds have small deep pharyngeal diverticulum dorsal to the larynx that can start to bleed profusely when penetrated. Additionally, over-inflation of balloon cuff might cause swelling, edema and obstruction of airways.

Pig Left Ventricle PV Measurement (Closed Chest) Cont.

Surgical Approach: Artery and Vein Catheterization

FEMORAL PERCUTANEOUS APPROACH

To facilitate access to the femoral canal, retract the rear hooves caudally with slight flexion of the hip joint and restrain them. For a percutaneous approach, locate the right femoral artery (RFA) by using anatomy landmarks and/or pulse palpation in the femoral canal or with the help of ultrasound guidance (USG). Use large 18-gauge, 2 3/4-inch Seldinger needle or trocar to percutaneously introduce it into the arterial lumen while advancing round tipped 0.038-inch Seldinger guidewire through the needle lumen into the RFA (Fig. 1). Withdraw the trocar from the skin. Do not damage the Seldinger guidewire. If under USG, examine position of the wire in the vessel lumen. Thread the dilator cannula through the guidewire into the RFA and advance it to desired position. A small incision might be necessary to insert the introducer past the dilator. Remove the Seldinger guidewire and introducer, leaving a blunt 7-10F cannula with blood sampling port in the RFA. It is advisable to use an access port at least 2 french sizes bigger than the PV Catheter. The cannula is sutured to skin to prevent movement (Fig. 2).

The femoral vein is located in the same adventitia, just medial to the artery. Use a similar method, as for the femoral artery, for cannula insertion. Use the LFV to insert the balloon catheter. It is best to use an access port at least 2F sizes bigger than the balloon catheter.

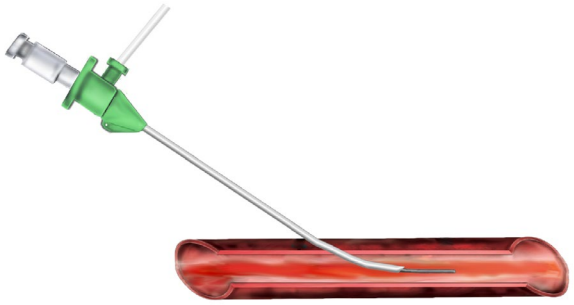

Fig. 1: Introduction of guidewire into the femoral artery using the Seldinger technique

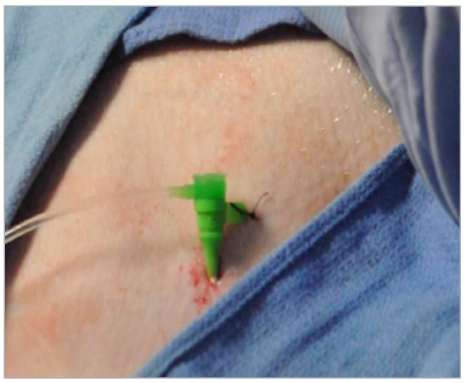

Fig. 2: Femoral vasculature access via percutaneous Seldinger technique

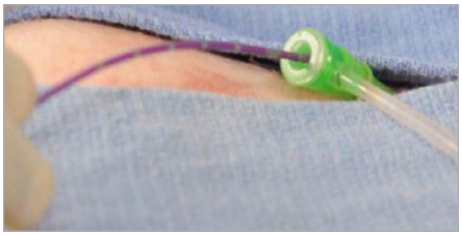

Fig. 3: Introduction of 5F pigtail pressure-volume admittance catheter into percutaneously catheterized right femoral artery (RFA)

FEMORAL CUT-DOWN APPROACH

The RFA and LFV are approached while the pig is placed in dorsal recumbence and the rear legs are retracted laterally. Pulsation of the superficial part of medial saphenous artery is identified in the skin fold between mm. gracilis and sartorius. Perform a skin incision cranial to this point using scalpel or electric cautery. Dissect the underlying subcutaneous tissue using blunt-tip scissors. Divide the fascia of mm. sartorius and gracilis using blunt-tip surgical forceps. Use self-retaining tissue retractor to further separate m. pectineus, while taking care not to damage the femoral nerve and vessels. Isolate the RFA for a length of 2 to 3 cm using blunt dissection.

PIG WEIGHT (KG)	BALLOON CATHETER SIZE	INSERTION APPROACH	DATE, AUTHOR, PMID
24-36	7 F	Left Fem. vein	2010, Filseth, 21926602
25-29	7 F	Open Chest	2012, Stenberg, 22307666
25-35	8 F	Right Fem. vein	2007, Kubitz, 17505303
27-30	14 F	Fem. vein	2013, Marshall, 23104696
31-44	7 F	RA	2002, Haney, 12151935
34.3-35.9	8 F	Fem. vein or ext. Jug. vein	2012, McCall, 22790084
38.3-43.1	8 F	Fem. vein	1998, Tayama, 9841537

Pig Left Ventricle PV Measurement (Closed Chest) Cont.

Surgical Approach Cont.

Rotate the beveled introduction needle to follow the contour of the RFA curvature. Insert the guidewire. The insertion needle is withdrawn. Thread the introducer through the guidewire into the vessel lumen. The blunt 7-10F cannula is passed over the guidewire into the widened RFA's lumen and advanced into desired position. It is advisable to use an access port at least 2 french sizes bigger than the PV Catheter. Attach the cannula with blood sampling port to surrounding tissue, restraining its movement.

The femoral vein is located in the same adventitia, just medial to the artery. Isolate the vein using blunt dissection. Secure 7-10F access sheet in the RFV. Confirm correct catheterization by withdrawing blood from both cannulas and run the blood gas from the RFA line, then flush the catheter with heparinized saline in order to maintain catheter patency. Flush the Catheter every 5-7 min. Secure both lines with 5-0 silk to skin that is closed with sutures. It is recommended to label the arterial and venous lines.

Use the LFV to insert the balloon catheter. It is best to use an access port at least 2F sizes bigger than the balloon catheter.

Fig. 4: 5F PV Catheter with straightening introducer retracted (top) and engaged (bottom) to uncurl pigtail.

FEMORAL APPROACH (PERCUTANEOUS OR CUT-DOWN) CATHETER INSERTION

The femoral approach uses the full length of the PV Catheter upon its introduction. The Catheter is introduced through a previously established Seldinger port. Manipulation of Catheter in the abdominal and ascending aorta and also in the aortic arch requires practice to limit vascular injury and induction of clotting cascade. Also, be cautious when manipulating Catheters inside pig arteries, since they are predisposed to vasospasms. Although the major difficulty while introducing the Catheter into the LV comes when the Catheter is passing through the aortic valve, other difficulties include its misplacement into the LCA and truncus brachiocephalicus. Use of fluoroscopy guidance for this femoral access introduction is essential. Note: Make sure there is not an excessive resistance present on introduction (vasoconstriction, vessel lumen distortion). If you encounter resistance, please stop moving forward and try to carefully pull back. Use fluoroscopy to determine the cause of an obstruction before the Catheter re-introduction.

With the 5F pigtail VSL Catheters, use the pigtail straightening introducer to uncurl the pigtail tip (Fig. 4). For 7F, straighten the pigtail with a guidewire. Ideally using 5F or 7F PV Catheters, there should be a very low amount of bleeding on introduction. For this remote LV catheterization, VSL Catheters with pigtail tip (both 5F or 7F) work best as the manipulation with a straight tip Catheter usually leads to its misplacement into the above mentioned vascular structures in the aortic arch. With the Catheter in the RFA, get the feel for the degree of resistance while gently rotating the Catheter. Manipulation of the pigtail Catheter in the aortic arch is easier because it can slide down along the aortic curvature. Also, in the final destination, the pigtail can be anchored more easily in the LV apex compared to a straight tip Catheter. If necessary, a 7F closed or open pigtail Catheter can be used with an internal guidewire to manoeuvre the tip through all above mentioned structures giving the user additional capability to make a sharp left turn in the area of the ascending aorta-at the origin of the aortic arch.

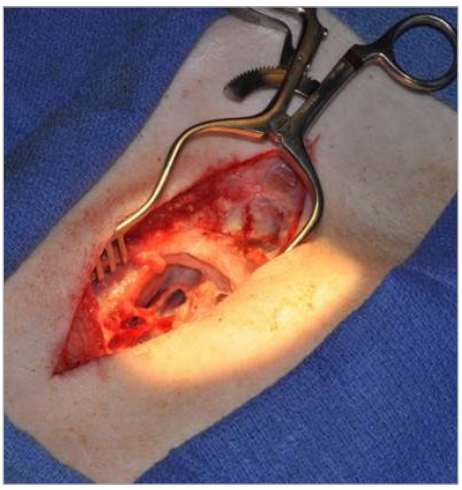

Fig. 5: Surgical site for right carotid approach

Note: If you choose to cut the end of 7F VSL closed pigtail Catheter to insert guidewire past the otherwise closed end, ensure that blood is not bleeding through the Catheter lumen. Position a hemostatic valve and/or stop cock at the end of the guidewire port.

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THE MEASURE OF BETTER RESULTS.

Pig Left Ventricle PV Measurement (Closed Chest) Cont.

Surgical Approach Cont.

RIGHT CAROTID CUT-DOWN APPROACH

Use a scalpel to make about a 9 cm skin incision perpendicular and medial to the line from the point of the jaw to the point of the shoulder. When using the el. cautery for dissection, please disconnect the PV Catheter. Use retractor to open the incision (Fig. 5). Use blunt scissors or medium hemostats to bluntly dissect an underlying glandular tissue from skin. Next, bluntly dissect the subcutaneous fascia and the fascial plane between the trachea and the sternohyoideus and the sternomastoideus mm to palpate the RCA pulse and localize the carotid adventitial sheath. Isolate using blunt dissection in order to prevent damage to the vagus nerve or its branch, the recurrent laryngeal nerve, that lies within the carotid sheath (Fig. 6). Also avoid damaging the nearby truncus sympaticus. Ligate/cauterize all arterial branches to reduce blood loss and minimize risk of dissection of the artery. Avoid major bleeding in the area. Minor bleeding can be stopped by digitally applied pressure on pre-cut gauze squares. Keep area moist with warm sterile saline or PBS.

Continue blunt dissection to expose the RCA to about 7 cm length. Dissect alongside the RCA distally towards the head. Ensure that section of the RCA is completely separated from all adjacent tissues to limit unexpected bleeding during the retraction and/or clamping procedures.

At this stage 2-0 silk sutures can be placed caudally around the RCA or internal jugular vein and ligated. To determine the anatomical location of this suture, please refer to Figure 9. Place the vessel loop to the caudal end on the RCA (close to sternum) isolated from its surrounding vascular fascia, to create tension.

Use sharp pointed scissors to make an arteriotomy (Fig. 7). A 0.038-inch guidewire is passed into RCA lumen (Fig. 8) before introducing a 7-10F blunt cannula (Fig. 9). The guidewire is then withdrawn. At this point the RCA has been retracted proximally and distally and cannulated (Fig. 10). The same process is repeated with the jugular vein.

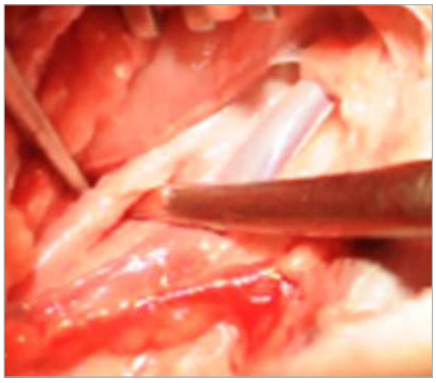

Fig. 6: Separation of the right common carotid artery

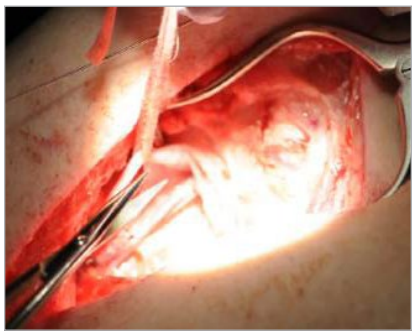

Fig. 7: Caudal control of the RCA is provided by lifting the vessel loop with exposed vascular segment in order to make an arteriotomy

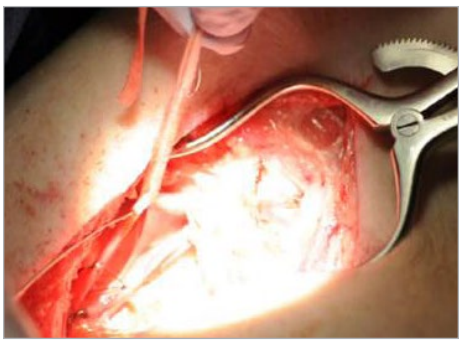

Fig. 8: Guidewire is inserted into the opening

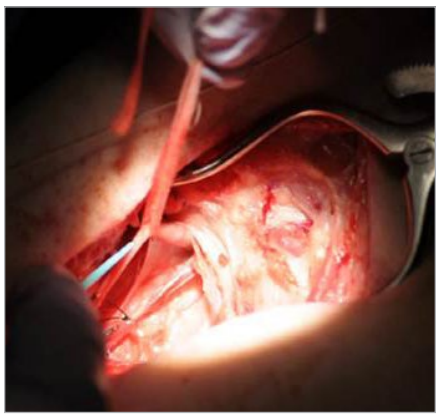

Fig. 9: Cannula is inserted over the guidewire and positioned, using the vessel loop

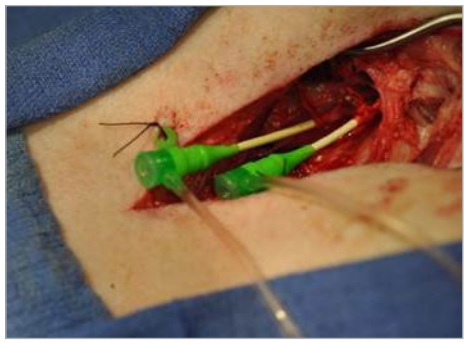

Fig. 10: Both the RCA and jugular vein are cannulated and ready for Catheter insertion

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Pig Left Ventricle PV Measurement (Closed Chest) Cont.

Measurement Procedure

CATHETER POSITION ADJUSTMENT IN LV

Before the Catheter reaches the LV, a typical arterial pressure tracing with dicrotic notch pattern, and a downward deflection on the down stroke of an arterial pressure waveform representing closure of aortic valve, can be observed (Fig. 11). On entering the LV cavity, changes in the pressure tracings occurs (Fig. 12).

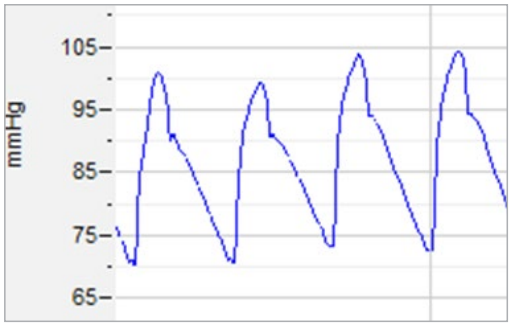

Fig. 11: Pressure trace in ascending aorta

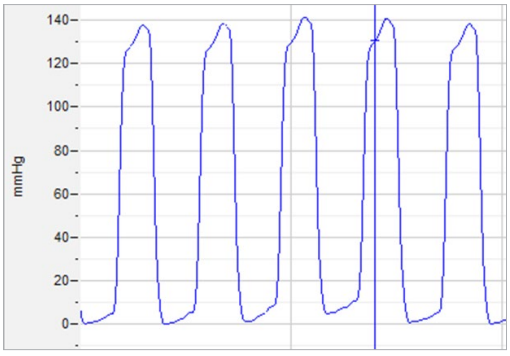

Fig. 12: Pressure trace in left ventricle

Allow the Catheter to stabilize in the LV for about 15 min before data collection. Crude adjustment needs to be made at this time based on phase angle (ɵ) and admittance magnitude (Y). Both signals should measure sinusoid wave signal. In the case of an off-center position, acquired sinusoid signals might be distorted (low amplitude, frequency etc.). Reposition the Catheter to stabilize and improve the signal. For more detailed description of Catheter positioning please see "Proper PV Catheter Placement in the Left Ventricle." Later, obtain end-systolic and end-diastolic blood conductance ($G_{b\text{-}ED}$ and $G_{b\text{-}ES}$) by turning the ventilator off for 15-20 sec. Every time after an adjustment (catheter position, ventilation, temperature etc.), re-record baseline PV. Record steady state values for at least 10 min for each animal before attempting IVC occlusion.

IVC OCCLUSION

Prepare the Fogarty balloon catheter and prime the inflation syringe with Iopamidol or similar contrast material. Inferior vena cava (IVC) occlusion is used to derive various load-independent indices of systolic function. Carefully insert the tip of the Catheter through the venous access port and pass the necessary length of Catheter shaft under the fluoroscopic guidance into the IVC. Localize the tip of the balloon catheter past the diaphragm (Fig. 14). Before inflating the balloon in the IVC, confirm its position by angiography.

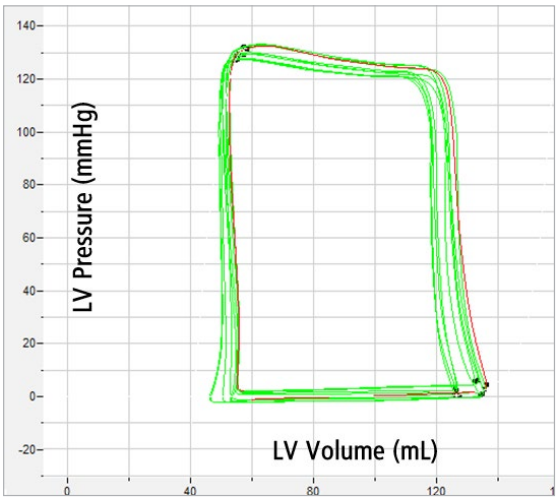

Fig. 13: Baseline (steady-state) PV loops for pig left ventricle.

Preload reduction: Before IVC occlusion, record pressure-volume steady state (Fig. 13). When the heart rhythm is stable, stop controlled mechanical ventilation and record baseline, uninfluenced by the lung motion artifacts. Record 5 sec of PV loop data and proceed to manometer- radio-opaque contrast dye balloon inflation to visualize the inflated balloon *in-situ* (Fig. 15). Its correct position is indicated by an immediate LV pressure and volume drop (Fig. 16). Deflate balloon and repeat these steps to obtain more than one stable occlusion, while allowing the pig to recover for at least 5 min between each IVC occlusion. If premature ventricular contractions (PVCs) occur during recording of baseline or IVC occlusion, exclude resultant PV loops. In the case of multiple incidents, all IVC occlusion recordings should be discarded and repeated.

Pig Left Ventricle PV Measurement (Closed Chest) Cont.

Measurement Procedure Cont.

While the animal is recovering from an IVC, promptly perform offline analysis of the preload reduction using data analysis software. Start the occlusion analysis at the point at which both systolic pressure and volume decline simultaneously and end at the point at which their decline reaches a plateau. Also pay attention to heart rate. Use data where HR does not change more than 30% from baseline during the IVC occlusion.

END OF EXPERIMENT

Terminate the experiment by carefully removing the PV Catheter by gently pulling it back through the access port. Please make sure that this manoeuvre is controlled, ensuring that the Catheter shaft that houses electronics is not overly extended. Insert Catheter tip into 20 ml saline centrifuge tube. Stop digital acquisition and save the data. Clean the PV Catheter as soon as possible according to proper care guidelines to considerably prolong the Catheter's life see "Cleaning Guidelines for Catheters."

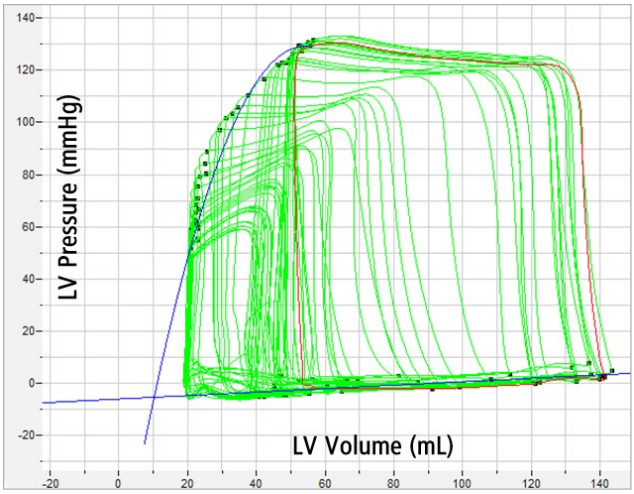

Fig. 16: PV loops during inferior vena cava (IVC) occlusion

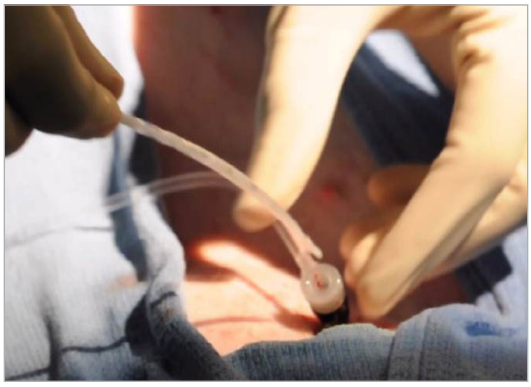

Fig. 14: Insertion of deflated Fogarty occlusion balloon catheter into the IVC through the percutaneous LFV access. The insertion port on the LFV access has to be at least 2F sizes larger to allow smooth access of the balloon catheter.

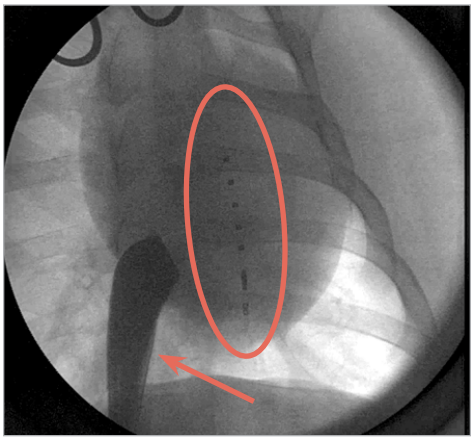

Fig. 15: Cardiac fluoroscopic image showing placement of pigtail VSL Pressure-Volume Catheter along the long axis of the left ventricle. Red arrow points to a 30 mm Fogarty occlusion balloon catheter that has been introduced through the left femoral vein (LFV) and inflated using Iopamidol to decrease preload during pressure-volume data collection.

ACKNOWLEDGMENTS

The study was approved by the Institutional Animal Care and Use Committee of the University of Nebraska Medical Center and was in compliance with the standards in the NIH Guide for the Care and Use of Laboratory Animals.

Provided material data and measurement courtesy of Dr. Shelby Kutty, MD, FACC, and Dr. Ling Li MD, PhD RDMS, Pediatric Cardiology, University of Nebraska Medical Center, Omaha, NE 68114, skutty@unmc.edu Tel: +1 402 516 6220 Fax: +1 402 955 4356.

Transonic Scisense Inc. also appreciates the expert technical assistance of John Lof, Elizabeth Stolze, Lucas Drvol of the Joint Cardiovascular Research Laboratory of the University of Nebraska Medical Center.

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PV Workbook RPV-5-wb Rev A 2014