Best-Practices to Achieve Quality PV Loop Data in Large Animal Models:
Webinar Q&A Report

Q: As large animal experiments are expensive, how best can I use this technology? Does it need to be a terminal study? Can I use this system serially in one animal?

[Transonic]: PV loops are performed as survival studies by many researchers. Results can be found in the literature.

[T. Hacker]: Yes, in large animals using percutanous access, most animal protocols will allow multiple procedures. We routinely do baseline PV loops before intervention/model creation and then again at the end of the study.

Q: I am doing VAD development… how is it best to utilize PV Loops and are there any specific challenges (surgically or related to data collection) that you can share?

[F. Konecny]: Please contact me directly to discuss (filip.konecny@transonic.com).

I believe that continuous detection of PV relationship along with detecting coupling on beat by beat basic will benefit any VAD development. We have longstanding experience with this topic, including empirical studies.

Q: How can PV Loops and admittance-technology be used best in the CORE lab? Dr. Hacker can you share your experience and approach to doing these types of large animal studies in your CORE?

[T. Hacker]: It is a selling point for us, since PV analysis is the gold standard for cardiac function and is much less expensive than MRI imaging (which is probably then next best method for assessment of cardiac function). Cardiac ultrasound can be difficult in pigs, better in dogs, and impossible in sheep. In addition, several other parameters can be measured by PV, (Ea, pressures etc) and PV analysis is better for testing acute interventions (dobutamine, other drugs). Since many of our procedures are catheter-based, it takes minimal effort to add PV loops to the interventions already performed.

Q: Can you share some tips and tricks, and general advice, for LV and RV apical stab approach?

[Transonic]: There are many tricks to be considered. Have been fortunate to have extensive training in swine bypass surgery and while working with the model I have learn that is important to not to make large stab wound(s) as this limits e.g. apical contraction when purse string is tightened.

Maybe as a resource there is great article about cardiac muscle mechanics like Buckberg's 2008 article in journal Circulation. There LV apex is describe to have a figure-8 configuration that form a vortex at the cardiac apex. These architectural anatomic description e.g. by Rushmer should be considered when performing stab.

Q: Can the effects of ventilation on the PV loops be used to derive the ESPVR?

[Transonic]: While this is an interesting theory, and might work, this is not a technique that Transonic Scisense has validated.

[T Hacker]: We typically don't get enough change in volume or enough beats in a row to get robust assessments.

Q: Is fluoro essential for LV PV catheter placement in open chest animal?

[Transonic]: No it is not. We have multiple clients not using fluoroscopy.

Fluoroscopy is a commonly used aid for catheter placement in large animals since the metal electrodes are visible under the x-ray scan. Depending on the application, fluoroscopy would not be considered *essential* for an experienced surgeon and may not be necessary at all in an open chest procedure.

Q: Have you found any difference using isoflurane vs sevorane in pigs? In any case, is only the gas anesthesia enough, or you will need also propofol or other drug drip?

[Transonic]: Yes, in terms of blood pressure drop. If I used 1MAC (1.2% for isoflurane vs. 1MAC for Sevo that approx. (2%) …at that time if I have paid attention blood pressures has dropped similarly however, Sevo is known that it can induce faster drop of systolic and diastolic BP at the beginning of the procedure. If I am using Sevo I had to pay attention of how much I deliver as I was used to using Isoflurane. Propofol might be seen in this case as desirable, but I tend to go about it by using less complicated approach…that is not combining injectables with inhalations. I have returned to Isoflurane for that reason.

1 MAC of Iso…1.2%, 0.5 MAC of Iso…0.6%

1 MAC of Sevo 2%, 0.5 MAC of Sevo 1%.

Q: How much variability could you expect in phase and magnitude when working with a hypertensive animal? Specifically in the Right Ventricle?

[Transonic]: Phase and magnitude values are variables used to calculate ventricular volumes. The resulting PV relations are then used to make observations of cardiodynamics.

Magnitude and phase by themselves are not meant to be indicators of a specific cardiac myopathy.

[T. Hacker]: We see phase slightly higher in the RV under all conditions, unless the hypertension has caused significant dilation of the RV, then it tends to be similar to the LV. The variability from animal to animal is pretty low (<10%), once the catheter is placed in an optimal position.

Q: What's the difference between an "over the wire" catheter vs the "pig tail" catheter?

[Transonic]: An “over the wire” catheter has a built-in lumen which allows the surgeon to use a guide-wire to aid in catheter placement and then pass the catheter “over the wire” and into position. A “pig tail” catheter terminates in a flexible loop which can be temporarily straightened using a guidewire or introducer. The choice between pig-tail or straight-tip catheter is both user and application dependent. For guidance, please consult our PV application workbook or your Transonic Scisense Research Specialist.

Q: Our dogs are typically around 10 kg. We almost always use seg 1. Is this normal?

[Transonic]: The goal of catheter sizing is to have the four relevant electrodes that comprise a “Segment” inside of the ventricle being observed. If the #1 segment is the one that fits in the ventricle of these dogs, then it is normal.

If you are always using the #1 segment, it might be worth checking to see if there is a catheter with a shorter #1 segment so that you have some room to maneuver if you encounter a smaller ventricle.

Q: How dies Dr. Hacker sterilize the PV catheters? What does Transonic recommend or authorize for catheter cleaning and sterilization?

[Transonic]: Catheters should be cleaned by soaking in an enzymatic cleaner. The recommended product is Tergazyme. http://www.alconox.com/product/cleanercatalog.aspx

Sterilization: As heat damages heat-sensitive materials such as electronics, and plastics (e.g. catheter handle), several commercially available cold disinfectant/sterilant chemicals can be used as an alternative. Most cold disinfectants/sterilants contain glutaraldehyde, which is available under several brand names. Please see (Table 1).

Please read the product information for a chemical disinfectant/sterilant before use. Chemicals vary in contact time, safety precautions, efficacy and the instrument compatibility. Instruments sterilized in this fashion must be in contact with the chemical for at least the minimum contact time (Table 1).

Each manufacturer of disinfectant/sterilant should be able to provide specific instruction and information regarding sterilant compatibility.

Important steps before Sterilization/Disinfection:

- Organic, non-organic debris and water can interfere with the effectiveness of the cold sterilization/disinfection. Please see Table 1 for usable shelf life after dilution or opening the container. Failure to observe such warnings inhibit the effectiveness of the process.
- Prepare/dilute the disinfectant/sterilant based on manufacturer's instructions
- Submerge the catheter into the disinfectant/sterilant up to the catheter handle. Please observe the temperature and time recommended. Do not submerge the catheter handle as it will damage the electronics and void the warranty.
- Wipe thoroughly the catheter handle with disinfectant/sterilant. Please observe the temperature recommended.
- Rinse 3-4 times with sterile water or saline (do not re-use sterile water or saline) to remove the chemicals prior to use to avoid irritating or damaging animal tissues

Table 1

Chemical Cold Disinfection	Brand Name	Dilution	Company	Minimum Contact Time Required	Shelf Life
0.55% Ortho-phthalaldehyde	Cidex OPA	N	ASP, Ethicon	12 min in 20-25ºC	14 days
0.6% Ortho- phthalaldehyde	Opaciden	N	Ciden Technologies	12 min in 20ºC	14 days
2.5% Glutaraldehyde	Rapicide	N	Cantel, MediVators	7 h 40 min in 35ºC	28 days
Ortho- phthalaldehyde	MetriCide OPA	N	Metrex	12 min in 20ºC	14 days

DO NOT USE:

- Glutaraldehyde solutions containing surfactants
  (e.g., Aldahol III, Metricide 28, Metricide Plus 30, Omnicide TM, Cidex 7 or Cidex Plus 28 Day)
- Solutions containing hydrogen peroxide (e.g. EndoSpor plus, SporoxTM)

Q: Are there any publications comparing continuous cardiac output from the PV loop with data measured by the thermodilution method?

[F. Konecny]: Not that I am aware of. Traditionally, the thermodilution technology is used to obtain the SV calibration parameter that is entered into the ADV500. Once the ADV500 is calibrated, it tracks the cardiac output and any subsequent changes in real time.

Studies have been done comparing the ADV500 data to echo and MRI results that show good correlation.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4001878/

http://www.ncbi.nlm.nih.gov/pubmed/23435903

http://www.transonic.com/resources/research/admittance-validation-porterfield-feldman/

Q: We have problems maintaining body temperature in our pigs. We cover the animals, have warm IV fluids and heating pads but often end up with cold animals... Any tips?

[Transonic]: Multiple institutions we have worked in use “Bair Hugger”. Various blankets are available for this specific unit.

[T. Hacker]: We generally use pigs 30-40 kg in size, so we normally don't have body temperature issues. We also use the Bair Hugger and have used heating pads above and below the animal with blankets.

Q: ESPVR and EDPVR values do not take linear relationships. Which analysis do you recommend for longitudinal studies?

[F. Konecny]: I would recommend software that can perform both calculations. When I analyze load-independent data I am also using e.g. SSE that is calculated for ESPVR curvelinear relationship, the sum of the squared differences between each observation and its group's mean. I used SSE to measure of variation within a cluster when performing comparison of individual occlusions and later I also use it for analysis between groups. EDPVR are in most cases (most software) calculated using non-linear relationship.

Q: Can this PV system be used in very large hearts – for example, bovines and horses?

[Transonic]: Yes it can. By using Wei’s equation to correct for the non-linear relationship between Conductance and Volume, it is possible to study large ventricles such as the horse or cow.

Q: I do experiments in conscious horses at rest and during exercise - would a moving animal significantly alter results?

[Transonic]: The challenge with doing conscious studies is stabilizing the catheter. A catheter that moves within the LV or is pulled out during moving will affect the volume data. The pressure signals are relatively immune to this as long as the sensor stays within the LV.

Q: How do you close the femoral vessel after removal of sheath in the survival procedure?

[Transonic]: manual compression when ACT decreases to less than 160-170 seconds in order to withdraw the sheet. When pulling the sheet off manually, pressure is placed on the femoral artery (usually 1-3 cm to the skin entry) then steady pressure is held for at least 15 minutes, then less manual pressure when applying a gauze or dressing. Larger the sheet (for the vessel size), longer the manual pressure applied.

Variety of collagen or PGA patches are also available to help to manual compression e.g. FISH i.e. the bio-absorbable ECM "patch" from swine intestinal submucosa.

[T. Hacker]: We only use manual pressure. Even in heparinized swine, we generally only need to hold pressure for less than 10 min.

Q: What is a normal value of Ees in pig?

[Transonic]: probably you do not want others that are cited elsewhere. I have measured these Ees in my experimental swine model studies (swine Landrace 63-70kg Ees ranges 2.93-4.23 mmHg/ml).

[T. Hacker]: We also see Ees ranges of 3-5 mmHg/ml. When stressed with dobutamine, we see these values increase to 4-7 mmHg/ml.

If you have additional questions for Dr. Tim Hacker, Dr. Filip Konecny or Transonic regarding content from their webinar or wish to receive additional information about solutions for PV Loop research and hemodynamic measurements please contact them directly:

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