T400-Series Technical Note

Keys to Successful Cardiac Output Measurements in Rodents

Common applications like the measurement of cardiac output can be challenging for the novice. Flow values that deviate from expectation may be difficult to understand and may arise from a combination of common errors. The following guidelines outline common pitfalls that affect flow readings and may present as "low" flow or "variable" flow measurement.

Target Vessel Position:

Ascending Aorta vs. Pulmonary Artery vs. Descending Aorta

Cardiac Output (CO) is the total blood flow output of the heart. It can be measured in the Ascending Aorta or the Pulmonary Artery. In small animals (rats & mice) the pulmonary artery is much less accessible for Flowprobe placement and is rarely used unless the investigation requires assessment of blood flow distribution to the lungs.

Cardiac Output in rats and mice is directly measured with a Transonic® Flowprobe placed on the ascending aorta, just before the aortic arch. This Probe position most completely captures the total outflow of the heart on each beat, less the blood flow that is diverted into the coronary circulation (about 10%).

Estimates of CO can be measured more distal on the lower thoracic aorta or descending aorta. However, the measurement will not include flow to the head in the carotid branches or flow in the brachial arteries and forelimbs, and so would be an underestimation of cardiac output. Placement of a Flowprobe in this position is less technically challenging than on the ascending aorta, and is sometimes used to detect relative changes in CO in experiments where entering the thoracic cavity would be too invasive and not pertinent to the study design.

Study Design:

Chronic Implantation

Although chronic implantation protocols present their own challenges, measurements with a previously implanted Flowprobe can be made under much more stable and physiological conditions than in an open chest experiment. It generally takes 3 – 5 days after surgery for fibrotic tissue to encapsulate the Flowprobe and ensure good signal quality. This period is also necessary for the animal to recover from surgery and affects of anesthetic agents. With the chest cavity closed and negative pressure restored, hemodynamics can be monitored for normal baseline conditions. Measurements may be recorded in the conscious animal, or under less potent anesthetics for dose/response studies. Note that cardiac output in the conscious animal will vary during the time of day in circadian cycle and activity level.

Acute Open Chest Descending Aorta

Measurements of cardiac output made in an acute, anesthetized, open chest protocol are lower and less stable than measurements made in an animal with an implanted Flowprobe. In the acute experiment, measurements may be technically compromised by Probe position and acoustic coupling to achieve good signal quality, but also by the physiological condition of the animal. The following parameters should be considered to optimize results.

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Anesthetic Agent May Depress Cardiac Output

Common anesthetics used for small animal surgeries include pentobarbitol, urethane, halothane, isoflurane and ketamine/xylazine. These agents can have a significant affect on cardiac output and the effect can vary between species. These also depend on whether the measurements are to be made in acute open chest application or after recovery from implantation in the conscious animal. Pentobarbitol is known to depress cardiac output in rats, but is often used for acute experiments and CO values are lower than expected. Ketamine/xylazine is a useful anesthetic for application in rats, but has severe and lingering effects in mice. Isoflurane has fewer systemic hemodynamic side effects in the mouse and seems to preserve cardiac function. Know the effects of the anesthetic agent on the study subject.

Maintain Body Temperature

A rat or a mouse loses core body temperature quickly when a body cavity is exposed during surgery. Measurements of cardiac output will drop considerably if core temperature is not maintained. We have observed flows that are 75% lower than typical reported values in open chest preps where the temperature has deviated 9° lower than normal (example: PA flow measured acutely in a rat: 16 ml/min @ 28°C; 40 ml/min @ 32°C; 60 ml/min @ 37°C). These dramatic affects are also reported in peripheral vascular flow measurements.

Temperature should be monitored and normal body temperature maintained during the experiment. Monitoring is easily achieved with a rectal temperature sensor. Heating pads or heated surgical platforms are available or can be easily constructed to provide adequate temperature control. A heating lamp light source can also be used. In both cases, be sure not to over heat the subject. Body temperature may also be conserved by covering the exposed area with gauze.

Ventilation & Appropriate Surgical Instruments

Working in a small animal model requires surgical instruments that are scaled down to smaller vessels than those used for large animal surgery. An excellent selection of microsurgical vessel dilators, forceps, scissors and other accessories are recommended and available from Fine Science Tools. See the recommended listing in our Technical Note RL-93-tn on our website www.transonic.com and in our "Tools and Techniques for Hemodynamic Studies in Rodents."

Animals that undergo open chest surgery must be ventilated mechanically with a respirator that will deliver the appropriate small stoke volumes and ventilation rates that are required by small animals. There are excellent products available for this purpose from Hugo Sachs Electronik and Harvard Apparatus.

Flowprobe Size Selection for the Ascending Aorta

It is important to choose the proper size Flowprobe for the animal species and strain that is used. Although Transonic® Flowprobes do fit a range of vessel sizes, the accuracy of the Flowprobe will be maximized in acute application if the Flowprobe fits the vessel more closely and the amount of gel required for acoustic signal coupling is therefore minimized. Transonic® surgical protocols recommend Flowprobe size by weight of the subject: for rats 250 – 350 grams: 2.5 mm Flowprobe; for rats < 250 grams: 2 mm Flowprobe; for larger rats 400 – 500 grams: 3 mm Flowprobe; a special 1.5 mm Probe configuration is made for a mouse ascending aorta.

Use of a larger Probe than necessary has two potential problems. First, a larger than necessary Probe may be too large for the anatomical space within the chest cavity and the space along the vessel. Secondly, the Flowprobe ultrasonic field is not 100% uniform. PS-Series Flowprobes tend to have greater sensitivity in the center of the Probe and less sensitivity on the edges of the Probe. We specify that the vessel should fill 75 – 95% of the Probe lumen to meet our accuracy specification. A vessel that is smaller than specified for a given Probe size will exhibit variable reading depending on the position of the vessel within the Probe .

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Probe Configuration & Surgical Approach:

Generally, the orientation of the Flowprobe cable with respect to the Probe head ("back", "side" or "lateral") is not as critical for acute open chest protocols as it is for chronic implantation where the cable must be tunneled subcutaneously to the midscapular area. However, the cable orientation influences how the Probe is positioned on the vessel.

Ascending Right Intercostal Thoracotomy:

Probe with lateral or side cable. This approach is less invasive but requires more careful dissection of the aorta because the vessel is almost hidden from view. See RL-18a-sp for details.

Median Sternotomy:

Probe with back cable. This approach is often preferred for acute measurements because the heart and aortic arch are easily visible. (RL-18c-sp).

Probe Position on the Vessel

The aortic arch presents a unique challenge to transit time flow measurement technology. Although Transonic® Flowprobes are largely insensitive to vessel alignment within the Probe, incorrect placement with respect to the aortic arch can have a large affect on the measurement values, causing an underestimation of flow by as much as 40%. Correct Probe position is essential to overcome this limitation: the plane of the Flowprobe ultrasonic path must be oriented perpendicular to the plane defined by the curvature of the arch for accurate flow measurement. Placing the Flowprobe so that the ultrasonic wave is in the same plane as the curvature of the aortic arch is incorrect and may cause readings that are lower than expected values. In practice, the Flowprobe will exhibit variable readings as the Probe is rotated on the ascending aorta giving the lowest reading on the curve and the highest reading when the Probe is placed correctly with respect to the arch.

Acoustic Signal Quality & Coupling Gel

An air bubble will block the ultrasonic signal and can cause variable or noisy readings. Acoustic signal coupling gel is supplied with the Flowmeter and should be used to displace any air that is trapped between the vessel and the Flowprobe. The type of gel that is used can also have an effect on the Flowprobe reading. Some ultrasonic gels affect the sensitivity of the reading and can contribute to a lowered measurement value. Transonic® recommends SurgiLube lubricating gel as an acoustic couplant because the acoustic properties of this agent match the acoustic properties of blood and will produce the least affect on the flow measurement. See Technical Note RL-9-tn for information about acceptable coupling gels.

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