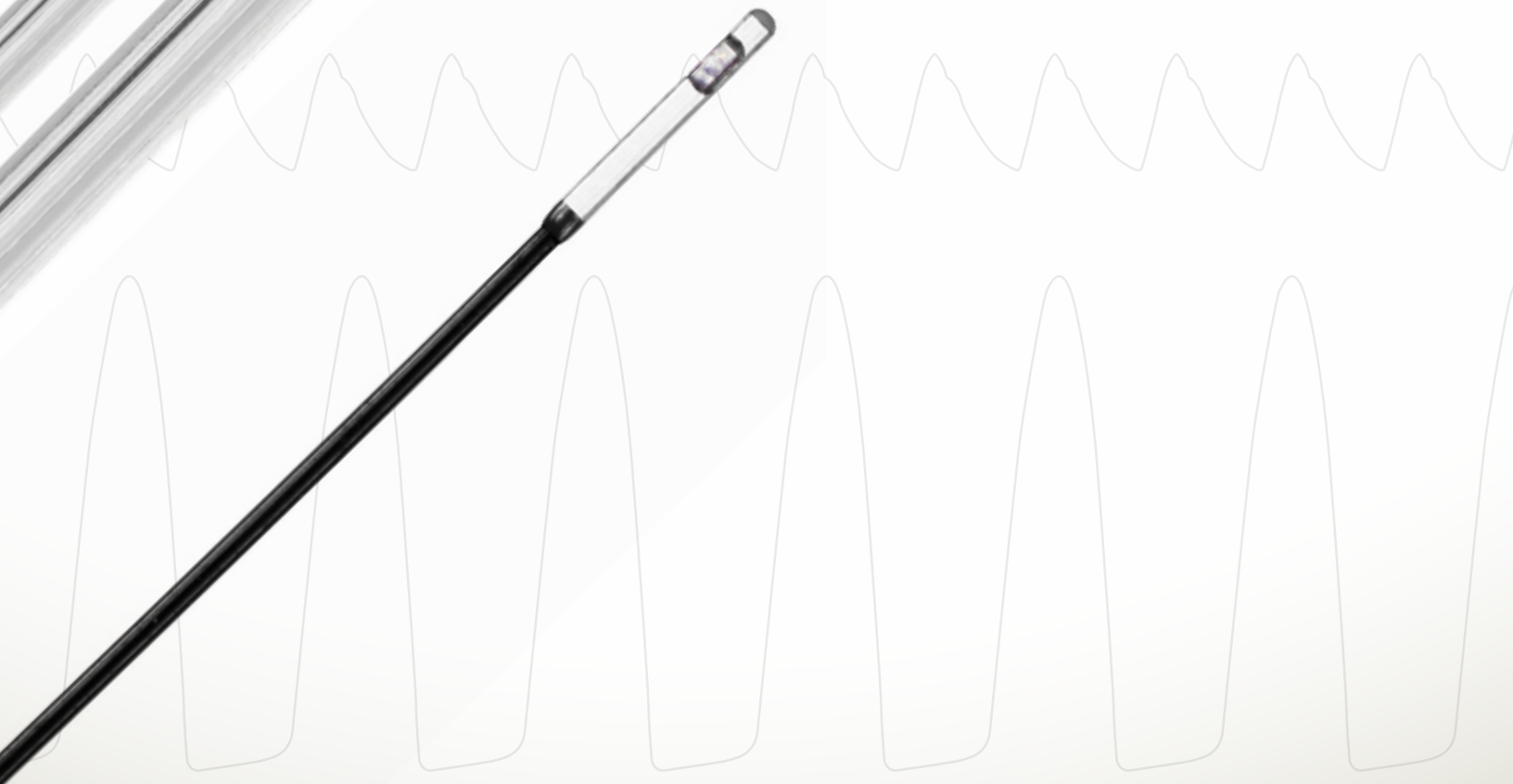


**HIGH-FIDELITY PRESSURE
MEASUREMENTS FOR
ANIMAL RESEARCH**



Accurate detection of blood pressure is perhaps the most crucial parameter in any study requiring an indication of cardiac function. In the research laboratory, pressure measurement techniques fall under two broad classifications: direct and indirect methods. Indirect methods, such as the Cuff Technique can be used to measure systemic blood pressure; however, these methods are approximate and cannot detect diastolic pressures accurately.

Direct pressure sensing devices offer a precise and meaningful measure of blood pressure and, as the name suggests, are able to detect pressure at the source. These devices are typically inserted (as part of a catheter) through the carotid artery or femoral artery until the sensor is located in the region of interest such as the ventricle or aorta. Solid state sensors, available from Scisense, are mounted at the tip of the catheter and measure pressure precisely and with a high degree of frequency response directly at this location. Alternatively, fluid-filled transducers rely on a liquid-filled tube to transmit pressure from the region of interest back to an external pressure sensor.

THE SCISENSE ADVANTAGE

The figures below show the difference in quality and accuracy of pressure detection between a Scisense solid state sensor and a conventional* fluid-filled sensor. Notice that the fluid-filled transducer is unable to accurately detect changes in pressure at higher frequencies. The signal becomes grossly distorted at a frequency of 5 Hz (approximately 300 BPM) and unrecognizable at 10 Hz and 15 Hz. In addition to measuring precise and noise-free pressure signals, solid-state transducers allow for accurate

detection and calculation of dp/dt , considered to be one of the most fundamental indices of cardiac function.

Furthermore, Scisense solid-state sensors are a user-friendly choice, as they do not require cumbersome and time-consuming flushing to remove air bubbles, nor do they involve a complicated system of tubing and stopcocks. Accuracy, reliability, and efficiency are Scisense advantages.

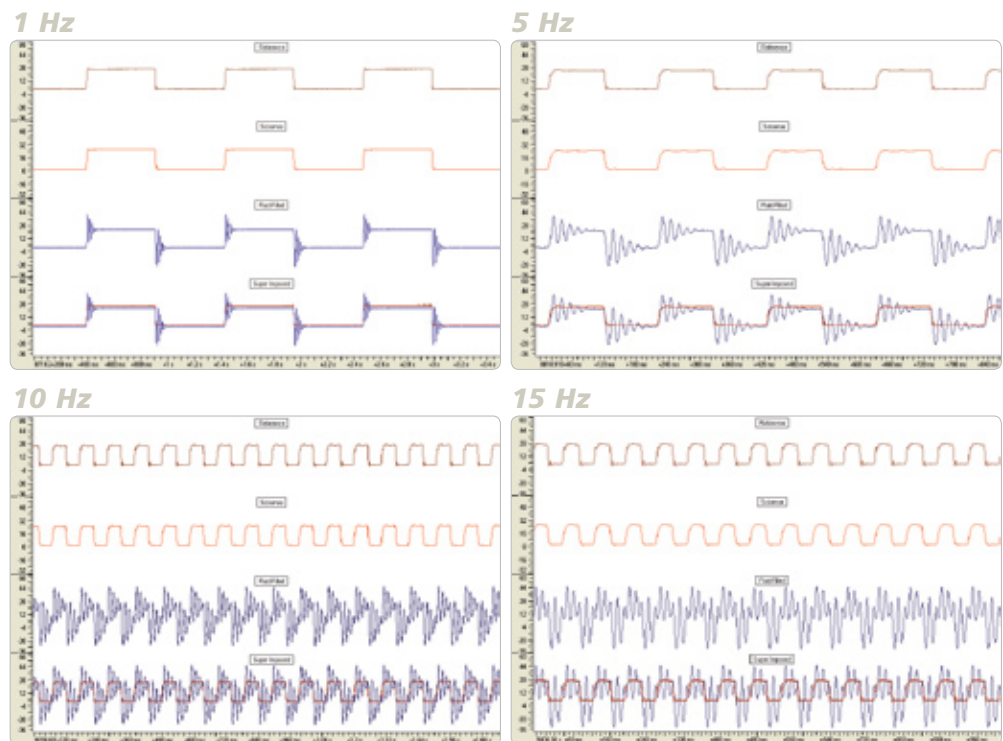
**Non-Conventional Fluid Filled Catheters, such as those used in implantable telemetry, were not included in this study.*

Signal Integrity:

- Square wave produced by a signal generator is accurately represented by the Scisense pressure catheter
- signal is distorted when measured by fluid-filled transducer
- above 4 Hz (equivalent to a heart rate of 240 BPM), the square wave is no longer recognizable with the fluid-filled sensor

Frequency Response:

- pressure amplitude is unaffected for Scisense transducer at higher frequencies but not the fluid-filled transducer
- at high frequencies, fluid-filled transducer cannot detect pressure changes accurately
- fluid-filled catheters require constant flushing as frequency response is affected by introduction of air bubbles into the fluid-filled system (catheter, stopcocks, tubing)



Comparison of pressure data recorded by reference pressure sensor (traceable), Scisense 1.2F pressure catheter and fluid-filled catheter (Cobe®) at 1 Hz, 5 Hz, 10 Hz and 15 Hz. Frequency response and signal integrity were evaluated.

OTHER BENEFITS TO SCISENSE SOLID-STATE PRESSURE SENSORS:

dp/dt :

- accurate detection of peak negative/positive dp/dt is dependent on true representation of pressure
- because of poor frequency response and signal distortion, accurate dp/dt will likely not be possible with a fluid-filled sensor

Signal Artifact:

- fluid-filled catheters are prone to whip and impact artifacts, while Scisense solid-state transducers are not affected by motion

Ease of use:

- fluid-filled catheters require constant flushing as frequency response is affected by introduction of air bubbles into the fluid-filled system (catheter, stopcocks, tubing)

Calibration and balancing:

- Scisense catheters are calibrated and balanced at any level prior to insertion, fluid-filled transducers require precise positioning when being calibrated

FUNCTIONAL PARAMETERS FROM SCISENSE PRESSURE SYSTEM:

| VARIABLE | DESCRIPTION | VARIABLE | DESCRIPTION | VARIABLE | DESCRIPTION |
|----------|---|-----------|---------------------|----------|---------------------------|
| NUM | Cycle Number | HR | Heart Rate | IVT | Iso Volumetric Time |
| Psys | Systolic Pressure | dP/dt min | Minimum dP/dt | TTI | Tension-Time Index Period |
| Pdia | Diastolic Pressure* | dP/dt max | Maximum dP/dt | Tau | Tau |
| Pmean | Mean Pressure* | CI | Contractility Index | Period | Period (ms) |
| EDP | Left Ventricular End-Diastolic Pressure | TTI | Time-Tension Index | PH | Pulse Height* |
| Pmin | Minimum Pressure | RT | Relaxation Times | TTPK | Time to Peak* |
| Pdev | Developed Pressure | NPMN | Non-Pulsatile Mean | %REC | Percent Recovery |
| | | Q-A | Q-A Interval | | |

* Asterisk denotes parameters calculated from arterial blood pressure analysis, all others are obtained by either arterial or ventricular pressure signal



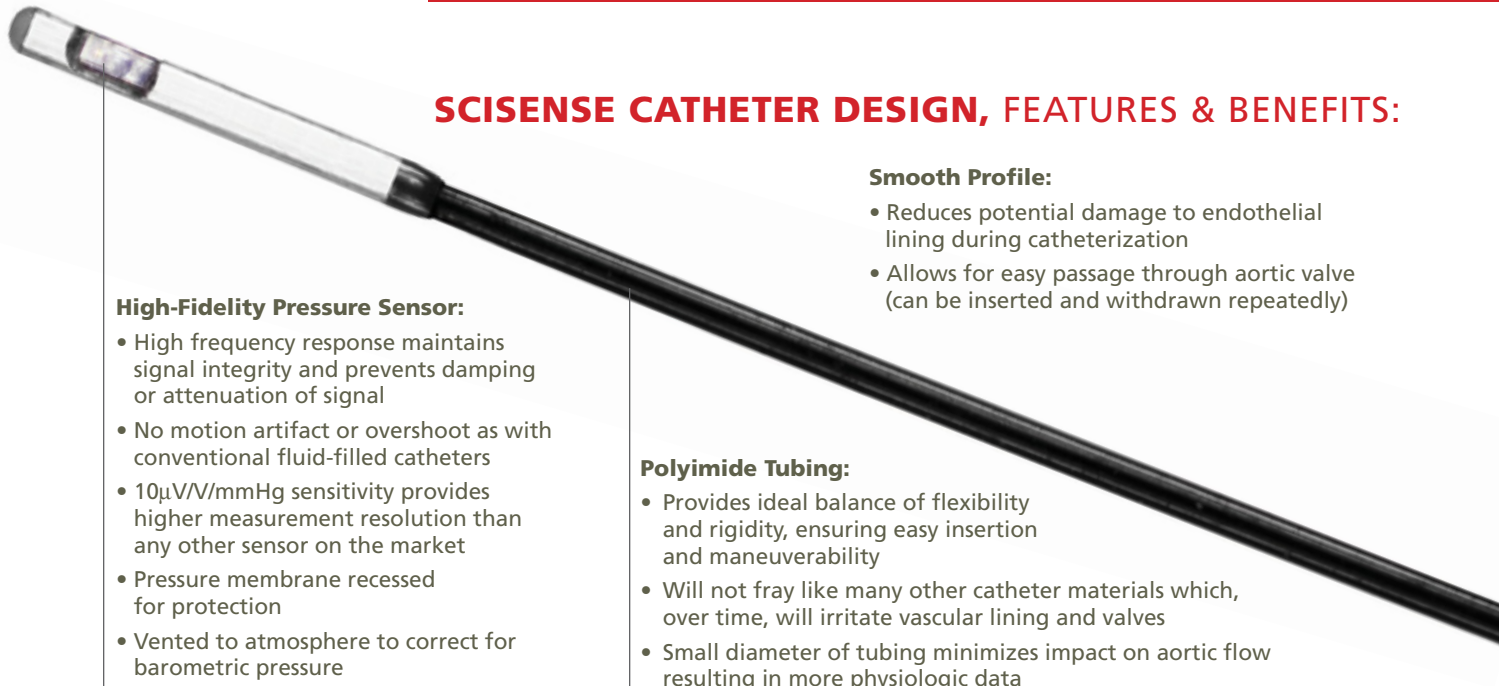
Pressure control box FP891

FP891 PRESSURE CONTROL BOX:

- 2-point electronic calibration with balance control for pressure
- Pressure output > 2V/100 mmHg, (no additional amplifier needed)
- Controls mounted on 15 degree angle for easy user access

2 channel version available

SCISENSE PRESSURE CATHETERS ARE COMPATIBLE WITH ALL OTHER COMMERCIALY AVAILABLE PRESSURE AND PRESSURE-VOLUME AMPLIFIERS!



SCISENSE CATHETER DESIGN, FEATURES & BENEFITS:

High-Fidelity Pressure Sensor:

- High frequency response maintains signal integrity and prevents damping or attenuation of signal
- No motion artifact or overshoot as with conventional fluid-filled catheters
- 10µV/mmHg sensitivity provides higher measurement resolution than any other sensor on the market
- Pressure membrane recessed for protection
- Vented to atmosphere to correct for barometric pressure
- Pressure and volume at the source from a single instrument

Smooth Profile:

- Reduces potential damage to endothelial lining during catheterization
- Allows for easy passage through aortic valve (can be inserted and withdrawn repeatedly)

Polyimide Tubing:

- Provides ideal balance of flexibility and rigidity, ensuring easy insertion and maneuverability
- Will not fray like many other catheter materials which, over time, will irritate vascular lining and valves
- Small diameter of tubing minimizes impact on aortic flow resulting in more physiologic data

Scisense manufactures a solid-state high-fidelity pressure sensor that can be mounted on catheters of all sizes. These pressure catheters are ideal for measuring systemic or cardiac pressures in rodents or large animal models. A variety of non-cardiac pressure measurements can also be obtained for urogenital, neuroscience and renal studies.

UNIQUE APPLICATIONS:

1. LANGENDORFF AND ISOLATED WORKING HEART MODEL

Isolated heart preparations allow for measurement of cardiac function without the influence of neurohormonal factors. Furthermore, the isolated heart model eliminates any impact anesthetics may have on function. These studies often incorporate balloon/fluid-filled type sensors placed inside the left ventricle; however, these devices are cumbersome to use and inherently lead to a poor quality pressure recording. An inaccurate pressure recording, and thus subsequent analysis of parameters like dP/dt , is attributed to:

- balloon non-conformity to the complex inner ventricle shape
- balloon compliance and its effect on accurate ventricle pressure transfer to the inner fluid
- how thin the balloon must be to accurately portray isometric wall tension, which also complicates construction and durability
- extension tubing which inherently complicates obtaining flat frequency responses at optimal ranges for rodent cardiac assessment (0.1 Hz – 1.0 kHz).

At the 3rd International Mouse Symposium in 2003, Sutherland et al. stated:

"The inadequate frequency-response characteristics of all such systems [balloon catheters] particularly limit the assessment of dP/dt_{max} and dP/dt_{min} . Such measurements in cardiac muscle typically require the high-fidelity recording of physiological pressure changes with component frequencies as high as 50-100 Hz. The error in these measurements is likely to be much greater and this throws doubt upon their validity as indices of contractile function... We would recommend that investigators using intraventricular balloons should recognize that such systems are unlikely, unless proven otherwise, to provide a reliable measure of $dP/dt_{max/min}$."

Scisense pressure catheters can easily be incorporated into Langendorff and working heart preparations in place of balloon fluid-filled style pressure sensors to obtain accurate pressure measurements and ensure proper calculation of pressure-derived parameters of cardiac function.

2. RODENT ECHOCARDIOGRAPHY AND SCISENSE LV PRESSURE CATHETERS

Many new echocardiography units offer the ability to input high level amplified pressure signals. Incorporating LV pressure measurements with echocardiographic images allows for the generation of pressure-dimension loops, including accurate determination of end-systolic and end-diastolic time points. Furthermore, simultaneous recording of blood pressure with echo imaging systems allows for vascular strain analysis. Conveniently, Scisense catheters interface directly with units such as VEO 770 from VisualSonics.

3. MEASUREMENT OF PRESSURE GRADIENT ACROSS AORTIC BANDS

Aortic banding is commonly used as a means to develop heart failure in the gene altered mouse. As part of this protocol, it is important to know what the pressure gradient is on either side of the band. Due to remodeling of the aorta, it is difficult to place even the smallest of high fidelity catheters in the aorta. Please contact us for more information.

4. TELEMETRY VALIDATION

Long-term recording of pressure has become increasingly popular in both the pharmaceutical and academic research settings. Implantable wireless pressure transducers are invaluable for these types of studies, but may exhibit some long-term drift. Scisense pressure catheters are commonly used during a telemetry study to validate that the pressure drift is within specification.

5. UROLOGY

Scisense pressure catheters can be used for a variety of urogenital applications. For example, catheters can be customized with multiple pressure sensors and electrical potential electrodes to simultaneously measure bladder pressure, urethral pressure and urethral EMG's. Please contact Scisense for more details about this custom application.


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MOUSE'N GENES

The mouse'n genes was conceived, as many great ideas, on a restaurant napkin. As a serious discussion around transgenic mice evolved, so did Sammy Scisense, as he is affectionately known today.

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