WHITE PAPER

Monitoring Vital Signs of Laboratory Mice and Rats During Surgery

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A Practical Approach

The use of mice and rats as surgical models for biomedical research represents an investment in resources for the scientific community. To improve chances for successful results, scientists strive to reduce the variables by closely monitoring and maintaining the animal's physiological status during surgery.

A new, innovative, compact device that combines different vital signs monitoring, artificial ventilation and anesthesia regulating functions specifically for mice and rats offers significant advantages to the scientific community. This is a critical factor in controlling the experiment.

A multi-functional instrument with modular components that share integrated digital operations and controls offers the following benefits:

1. Provide the ability to rapidly learn operating functions with a simplified user interface
2. Accurately monitor and maintain physiological variables
3. Improve surgical outcomes
4. Capture experimental data documentation
5. Save valuable and limited surgical space with a significantly smaller system

Introduction

Laboratory mice and rats have physiological characteristics that confound clinical assessment such as smaller organs, faster heart rates, and reduced respiratory volumes. Historically, the approach to developing physiological monitoring equipment for laboratory mice and rats has been to adapt or modify instruments designed for human use.

A number of different devices are available to assess and respond to sudden changes in body temperature, heart rate and respiration during anesthesia and surgery.

Temperature sensors with warming devices regulate body temperature and pulse oximeters assess oxygen uptake in arterial blood and measure heart rate. Capnographs measure end-tidal carbon dioxide ($ETCO_2$) production, which is useful for assessing respiratory function, and ventilators provide breathing assistance.

Typically, each function is performed using a different device that adds to the operational complexity and the cost of research. While electronic monitoring equipment should never replace human clinical observation, some devices are capable of outperforming humans by maintaining continuous observation of the animal, and by measuring parameters that humans are unable to detect and quantify reliably. Electronic monitoring equipment provides uninterrupted monitoring allowing scientists to track trends and be alerted when physiological parameters are out of bounds. This is far more valuable than intermittent, visual observations.

By performing accurate and continuous assessment of the animal's body temperature and heart rate, and by controlling the animal's respiratory function, a higher rate of success for surgical procedures is permitted. Better research results occur when investigators control experimental variables.

The objective of achieving reproducible results while conserving research resources is important for scientific, humane and economic reasons.

A New, Practical Approach

A multi-functional system using individual modules for measuring the animal's vital signs is available. The pulse oximeter module measures the animal's oxygen saturation level (SpO_2), heart rate (HR) and respiratory rate (RR). The capnograph module measures expired or end-tidal CO_2. The warming module measures the animal's core body temperature and provides homeothermic warming to maintain the temperature at the desired level. A module developed to provide artificial ventilation assists in the animal's breathing during surgical procedures.

This new design allows the modules to be operated individually or combined, and has integrated digital controls with a shared real-time display. Compact in size, the system dimensions are 20.3cm wide by 7.6cm high by 15.2cm deep (8in wide by 3in high by 6in deep). Vital signs information is displayed immediately providing the researcher with the opportunity to rapidly respond to unsafe conditions during surgery.

In addition to real time data, previously collected data can be displayed with the touch of a button. There is no need to connect to an external computer to operate the system. The system incorporates a self-contained microcontroller and integrated screen to provide numeric readings and waveforms. Simultaneous measurements can be easily displayed on the single screen. The system interfaces with an external computer to allow data transfer for statistical analysis or electronic documentation.

The functional design of the system accommodates the high heart rates, low respiratory volumes, and thin vascular beds of mice and rats. By using technology specifically designed for rodent physiology, scientists continuously and accurately monitor the animal's vital signs, which leads to a vast improvement in surgical outcomes, with better research results.

Pulse Oximetry and Heart Rate

Although essential, the measurement of arterial blood oxygen saturation is neither required nor is it routinely performed with mice and rats under anesthesia. Equipment cost is often cited as the primary reason. Most monitoring equipment is either too large or not sensitive enough to accurately measure oxygen concentration in rodents, especially mice.

Vital signs monitoring during surgery is critically important for gauging the depth of anesthesia, maintaining the animal's safety, and preserving the validity of the experimental data that are generated from the surgical procedures.

The pulse oximeter module has a sensor that uses a photoreceiver and a photodetector to pass two wavelengths of low intensity light through the animal's body tissue. The signal is digitally processed to obtain the oxygen saturation measurement.

A uniquely designed paw sensor provides the researcher with an accurate indication of the animal's blood perfusion, more reliably and quantifiably than mere clinical observation. Heart rates up to 900 beats per minute (BPM) can be accurately obtained with this system.

The system's pulse oximetry measurements have been clinically validated by comparison to blood gas readings.

Temperature Monitoring and Control

Mice and rats under anesthesia have difficulty regulating their internal body temperature since they have a high surface area to body mass ratio.

The risk of hypothermia poses great harm to the safety of the animal, as well as challenges to vital signs monitoring during surgery. In addition, surgical procedures such as inhalation of cool anesthetic gas, preparative hair shaving, opening of body cavities, and rapid water loss and dehydration further impact the animal's ability to maintain normothermia during surgery and post-surgical recovery.

The system provides the capabilities for temperature monitoring and homeothermic control in a single module. The homeothermic controller component employs thermistors to accurately monitor animal core body temperature. The temperature of the far-infrared warming pads is automatically adjusted to maintain the proper body temperature.

Far infrared warming technology (FIR) warms the animal at the core body level instead of dangerously heating the animal's skin surface as done with traditional warming devices. Far infrared heat is absorbed deeply within the animal's body to safely warm the animal. The core body temperature is maintained without heating the air between the FIR source and the animal. Internally, the energy level of water in the body is gently increased through "resonant absorption" thereby warming the body core.

The animal's body can absorb as much as 90% of the FIR warmth compared to only 20% with conventional warming devices. Research studies have shown that FIR can maintain therapeutic temperatures much longer when compared with conventional heating methods. With FIR researchers can warm the animal for longer periods of time without fear of overheating.

Digital Ventilation

For most surgeries, the animal would greatly benefit by the use of a device to provide breathing assistance during the procedure.

Traditional ventilation systems for small animal anesthesia are not well suited for the low respiratory volumes common to mice and rats. As freestanding systems, these large machines occupy substantial bench space and require continuous maintenance.

The automated ventilator module is integrated with the other monitoring modules in the new system. The module provides robust ventilation for deeply anesthetized animals and a less robust ventilation for lightly anesthetized animals that require assistance with spontaneous breathing.

The automated ventilator allows the researcher to easily enter the animal's weight. An allometric formula automatically determines a suitable tidal volume and respiration rate for the appropriate artificial ventilation.

The ventilator module is operated in either a pressure-controlled or volume-controlled mode, offering the user convenient choices in operating parameters to assure animal safety. Delivery of vaporized anesthetic to the animal through the inspiratory tubing line improves sensitivity and precision.

For open chest surgery, the peak end expiratory pressure (PEEP) function is essential and provides the necessary back-pressure to prevent the collapse of the animal's lungs.

The automatic Sigh Breath helps avoid atelectasis by causing the redistribution of the surfactant in the alveoli.

Measurement of Exhaled CO_2

The decision to continually assess animal health during anesthesia should include the evaluation of expired CO_2 (capnography) which provides metabolism, circulation and ventilation information.

While visual observation of the animal's chest has sufficed for many investigators, capnography equipment provides continuous and accurate status of cardiopulmonary performance. Early detection of hypoxia, hypercapnia, hypothermia, and other deleterious conditions have a direct impact on the outcome of the experimental procedure.

Capnography equipment that is designed for humans and adapted for small animals is too large for the surgical field and ill-suited to properly assess the low flow rates common in mice and rats.

The new capnographic module measures end-tidal CO_2 ($ETCO_2$) in real-time, using infrared absorption spectroscopy. A sidestream or diverting capnometer transports a sample of the animal's respired gases to a carbon dioxide specific measuring sensor.

To increase the accuracy of the measurement, close proximity of the CO_2 sensor to the animal's airway is necessary. The CO_2 value is plotted against time to reflect the partial pressure of carbon dioxide within the animal's airway in real time.

There are three modes of data output; (1) averaging, (2) instantaneous, and (3) comparison of millimeters of mercury (mmHg) to expired CO_2 percentile.

Instrument settings allow users the flexibility to compensate for changes in temperature, pressure, and the presence of other gases such as O_2, N_2O, helium, and anesthetic agents in the gas mixture. When the CO_2 sensor is calibrated to zero, the calibration is stored in system's memory.

Conclusion

As an integrated module, capnography in addition to the other three modules, pulse oximetry, temperature monitoring/regulation and automated ventilator modules provide an improved assessment of the physiological status of the animal under anesthesia.

Laboratory animal surgery must adhere to regulations disseminated by society's concerns to maximize the animal's health and minimize the danger of anesthesia exposure. Today's economy places financial pressure on laboratories to conserve time and resources while maintaining safe, surgical research.

A compact vital signs monitoring system designed to manage the physiological conditions of small animals under anesthesia can address these challenges and provide the following advantages:

- Clear and continuous monitoring of the animal's health status
- Efficient use of time and money
- Improved care for the animal's well-being
- Proper guidance for the surgical team

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Traditional Monitoring Equipment

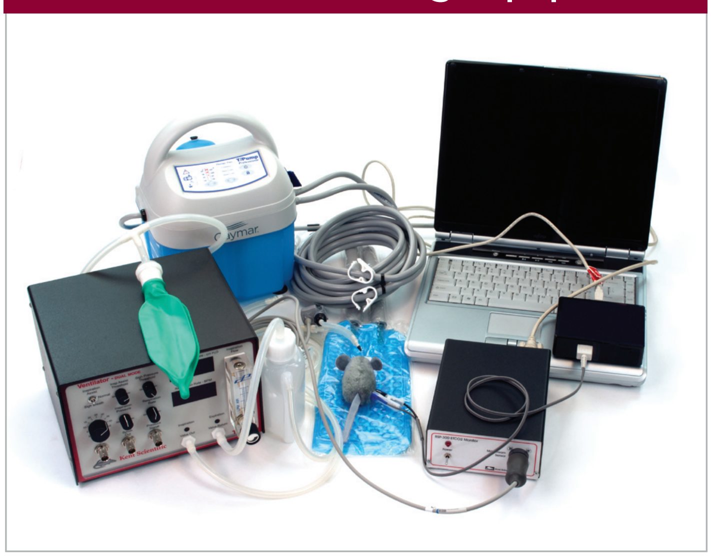

Image 1: Traditional monitoring devices for pulse oximetry, heart rate monitoring, artificial ventilation, $ETCO_2$, and temperature monitoring and warming occupy significant bench space.

A New, Practical Approach

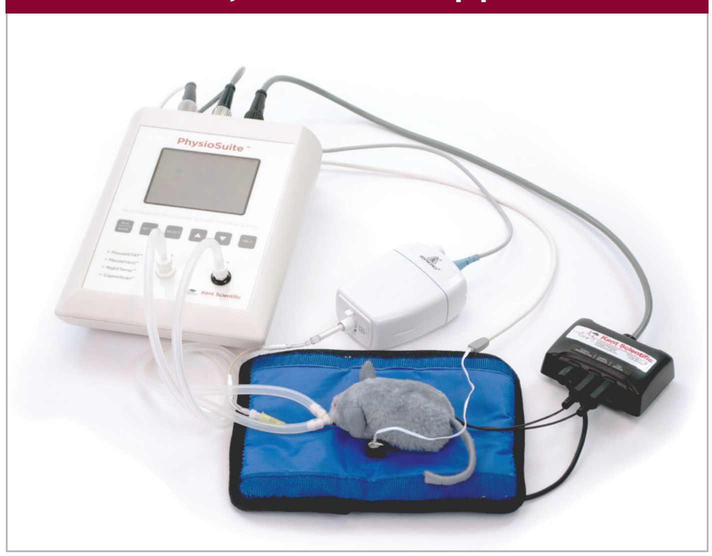

Image 2: This compact system with modules for pulse oximetry, heart rate monitoring, artificial ventilation, $ETCO_2$, temperature monitoring and homeothermic warming save a significant amount of space in the surgical area.

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