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New Device for Noninvasive Telemetric Monitoring of Vital Signs in Healthy and Newly Operated Piglets

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Measuring vital signs is central to medical practice, but they are difficult to monitor in awake laboratory animals. We examined the feasibility of a noninvasive device for telemetric assessment of respiration rate, heart rate, temperature and movement in pigs. Awake piglets were monitored continuously for 31 h (interquartile range, 7) before (n = 4) and after (n = 3) surgery. Data quality was sufficient for determination of all parameters. We conclude that continuous, noninvasive monitoring of pigs is possible by using the evaluated device.

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Routinely, vital signs are acquired to diagnose disease and assess its severity.[3] Respiration rate, heart rate, and temperature are physiologic hallmarks, but long-time monitoring is difficult in awake laboratory animals. Frequent examinations are resource-consuming and biased due to the presence of the investigator and the stress of handling.[5,9] Therefore, researchers often do not assess the vital signs of laboratory animals between procedures.

Noninvasive devices could solve this issue.[6] However, previously used devices were bulky, required surgical implantation, or provided only few data, such as heart rate without an electrocardiogram.[2,6-8] In recent years, telemetric technology has evolved, and new devices may overcome these limitations. One such device is the commercially available Cortrium C3 (Figure 1). Designed for humans, it acquires an ECG, respiration curves, surface temperature, and accelerometer data.

We hypothesized that noninvasive telemetry using this device would provide easy and reliable, long-time monitoring of vital signs in large animal research. Therefore, we aimed to investigate the validity and feasibility of using this device for pre- and postoperative monitoring in pigs.

Materials and Methods

All experiments were approved by the Danish Animal Inspectorate and were performed in conformation with Danish legislation. We used healthy female Landrace piglets (*Sus scrofa domesticus*; n = 8; age 14 to 16 wk; weight 40 to 60 kg) obtained from a conventional supplier. The pigs were housed in SPF facilities, kept in small groups in enriched pens (12:12-h light:dark cycle), and were given free access to water but had a restricted diet (2 to 2.5 kg growth/week).

Monitoring device. The C3 (version B8; Cortrium, Copenhagen, Denmark) is a single-unit device (80 × 80 × 17 mm, 30 g) with 3 mount points for ECG electrodes. The ECG sample rate is 250 Hz, whereas impendence-derived respiration, temperature, and accelerometer data are recorded at ~42 Hz. Real-time monitoring is available through a smartphone, and 48 h of data are recorded.

Validation. To validate the device, we tested heart rate by measuring against a reference. In piglets anesthetized similarly to that described later, we simultaneously recorded the heart rate as determined by the vendor-supplied smartphone application and a clinical-grade anesthesia monitor equipped with a pulse oximeter (GE Healthcare, Wood Dale, IL). Recordings were obtained every 5 s for several minutes from 8 pigs.

Monitoring before and after surgery. To test the relevance of the device to researchers, we tested the device before and after a small surgical procedure in the same animals. Before the start of the experiments, the piglets (n = 4, 15 kg) were acclimated for 14 d. Two days before surgery, a device was fixed under sedation (5 mg/kg IM tiletamine and 5 mg/kg IM zolazepam, Virbac, Kolding, Denmark). The device was attached to the left of the spine, covered with adhesive tape, and fixed by bandaging the thorax. The animals were bandaged with care to avoid restriction of breathing.

After preoperative monitoring, the piglets underwent a 1-h procedure to cause pulmonary insufficiency.[1] Through a 3- to 4-cm thoracotomy, the anterior pulmonary valve leaflet was blindly plicated by suturing through the pulmonary trunk. The following drugs were administered: 0.5 mg/kg IM midazolam (Matrix Pharmaceuticals, Hellerup, Denmark) and 0.5 mg/kg IM azaperone (Elanco Animal Health, Herlev, Denmark) as premedication; 3 mg/kg IV propofol (Fresenius Kabi, Copenhagen, Denmark) for induction of anesthesia and 3.5 mg/kg/h IV for maintenance; and 0.025 mg/kg/h IV fentanyl (Matrix Pharmaceuticals) and 2 mg SC bupivacaine per cm of wound (AstraZeneca, Copenhagen, Denmark) as analgesia. Heart rate and expiratory CO_2 were monitored. Rocuronium (1 mg/kg IV; Matrix Pharmaceuticals) was administered at deep anesthesia. After surgery, the device was reattached to the piglet. The animals were kept at the surgical facilities overnight before transportation to the farm, by when the pigs were eating and moving freely. The device was removed after 48 h. Agents

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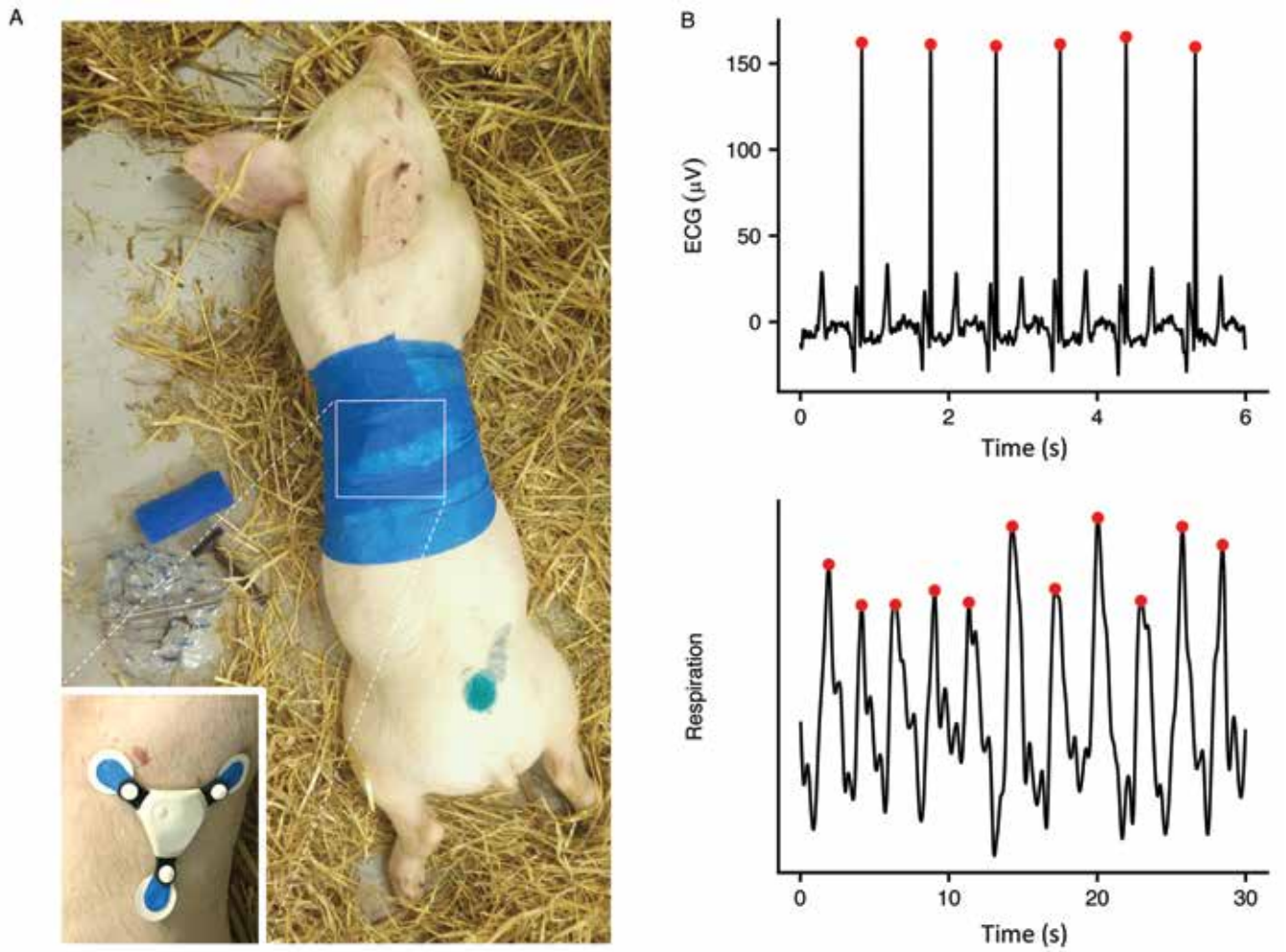

Figure 1. (A) The monitoring device is secured to the posterolateral thorax. (B) Filtered ECG and respiration signals from an awake animal. Data was of best quality when animal activity was low. Dots mark detected peaks.

for postoperative analgesia and infection prophylaxis were 20,000 IU/kg penicillin (Boehringer Ingelheim, Ingelheim am Rhein, Germany), 250 mg ×2 acetaminophen (GlaxoSmithKline, Denmark) and 0.4 mg/kg meloxicam (Boehringer Ingelheim) administered IM daily for 5 days. The animals were exsanguinated under anesthesia as described earlier.

Data analyses. The data from the monitoring of awake pigs were converted to CSV file format using vendor-supplied software (Cortrium).The ECG and respiration signals were filtered by using a forward-reverse Butterworth bandpass (respiration, 0.5 to 10 Hz; ECG, 1 to 30 Hz) and a running-medians filter. A peak detection algorithm was applied. Animal activity was defined as the absolute value of accelerometer magnitude minus the gravitational acceleration. Analyses were performed by using the R environment. All data were averaged over 1-h periods to correct for inaccurate peak detections and to facilitate visualization.

Results

Validation. The heart rate measure of the telemetry device showed good agreement with a clinical pulse oximeter across a variety of heart rates (Figure 2; Bland–Altman plot of 633 observations from 8 pigs).

Monitoring before and after surgery. All recordings in awake pigs were successful, except for one animal in which the device detached. The median duration was 31 h (interquartile range, 7; number of recordings, 7), which was limited by battery life or

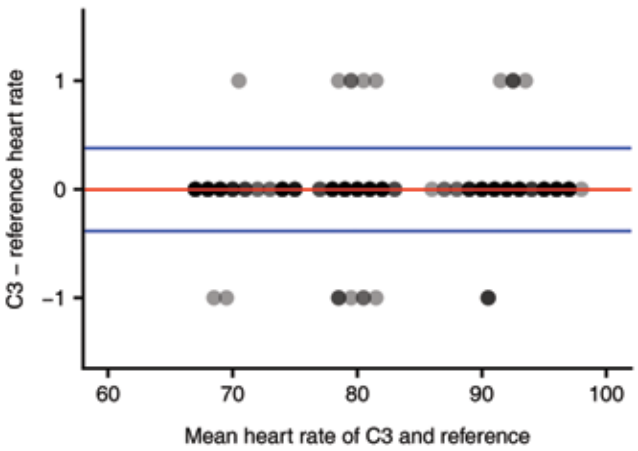

Figure 2. (A) Bland–Altman plot comparing the heart rates of 8 anesthetized pigs measured by using the new device compared with a pulse oximeter. The heart rate was recorded every 5 s, yielding a total of 633 observations.

device loosening. The signal quality was best during the night (Figure 1). In the daytime, we found few motion artifacts that disturbed respiration signal peak detection. Data quality was generally sufficient to perform analyses.

Data from vital sign monitoring are shown in Figure 3. Before surgery, heart rate was 90 to 120 bpm, the temperature was 36 to

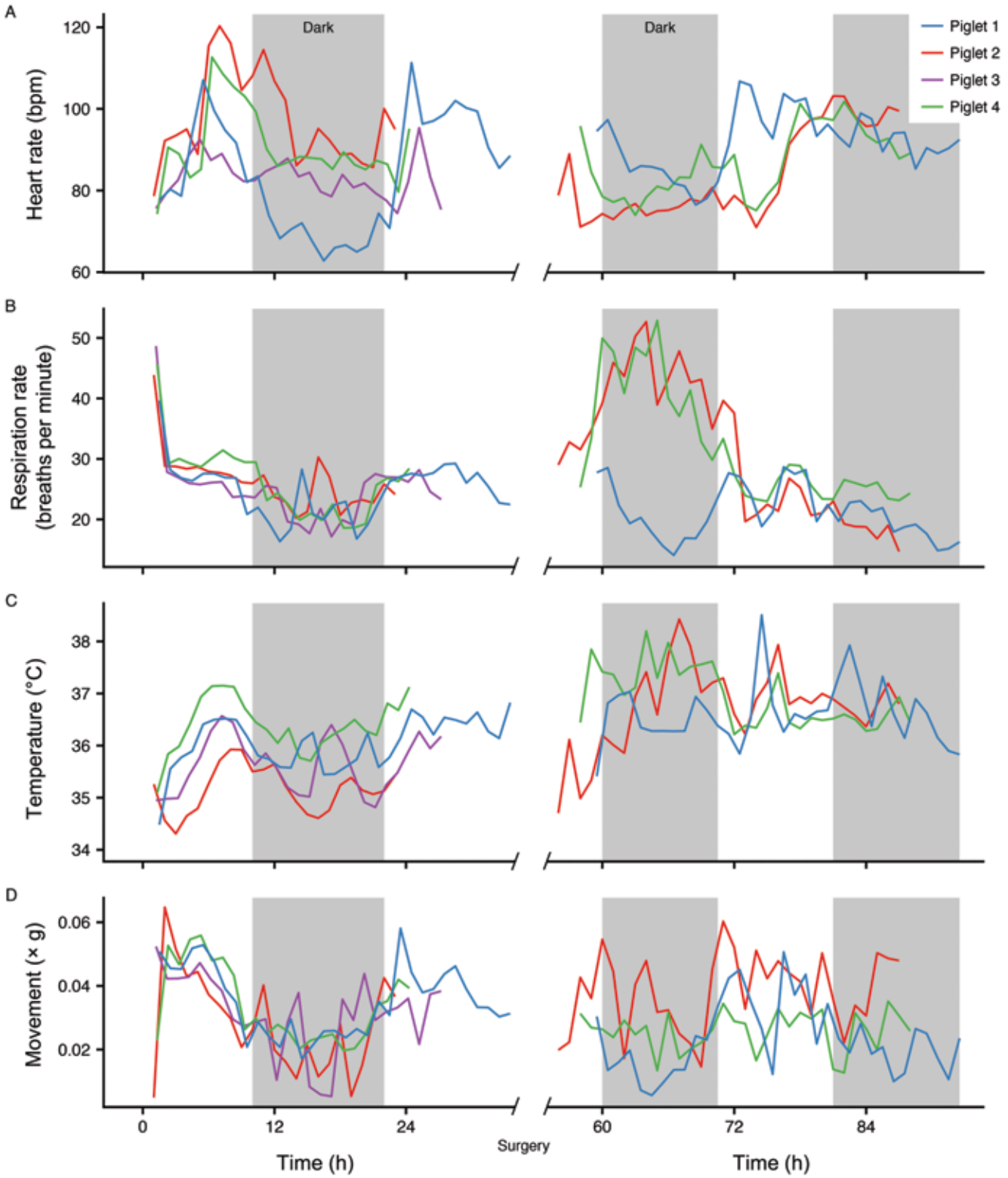

Figure 3. Noninvasive monitoring of vital signs before (n = 4) and after (n = 3) brief surgery in piglets. The break in the x axis indicates when surgery was performed. (A) Heart rate. (B) Respiration rate. (C) Surface temperature. (D) Accelerometer-derived movement. Data are presented as means over 1-h periods.

37 °C, and the respiration rate was 28 to 30 breaths per minute. Sedation for device fixation increased the respiration rate to 40 to 50 breaths per minute and briefly decreased heart rate to approximately 80 bpm. All parameters varied with the light:dark cycle (heart rate, approximately 20 bpm; respiration, 10 breaths per minute; temperature, 2 °C; and movement, 50%). After surgery, the heart rate increased to normal levels overnight, from approximately 80 to 100 bpm. Two piglets became dyspneic (40 to 50 breaths per minute) for 10 to 12 h after surgery; the third piglet breathed at a normal rate.

Discussion

The aim of this feasibility study was to evaluate a new monitoring device (C3, Cortrium) in an experimental animal model. We found the device easy to use; it provided reliable data and did not seem to stress the piglets. Our results are comparable to the normal values for immature pigs.[4]

Vital signs are early markers of postoperative complications.[3] In the current study, the parameters monitored seem to be clear markers of stress due to surgical trauma. Real-time assessment of vital parameters could refine animal research by allowing early intervention.[5] Furthermore, the recorded data could be valuable in models of disease or in toxicology research.

Noninvasive telemetry on freely moving animals can facilitate the monitoring of vital signs without inducing stress. However, correct interpretation of the data depends on the circumstances under which telemetric data are obtained (that is, resting, eating, or sleeping). Continuous recording allows personnel to evaluate long periods of time and account for circumstantial changes. Furthermore, the simultaneous measurement of animal movement assists in the analysis of the other parameters, and periods of excessive movement could be excluded, ensuring comparable animal activity levels and minimizing motion artifacts. If elimination of sedation or more than 48 h of data is required, animals could be trained to accept device fixation.

In conclusion, we demonstrated the feasibility of a new commercially available device for noninvasive and continuous monitoring of ECG, respiration, surface temperature, and movement in awake pigs.

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