Investigation of a novel thermal support system to recover post-anesthetized mice

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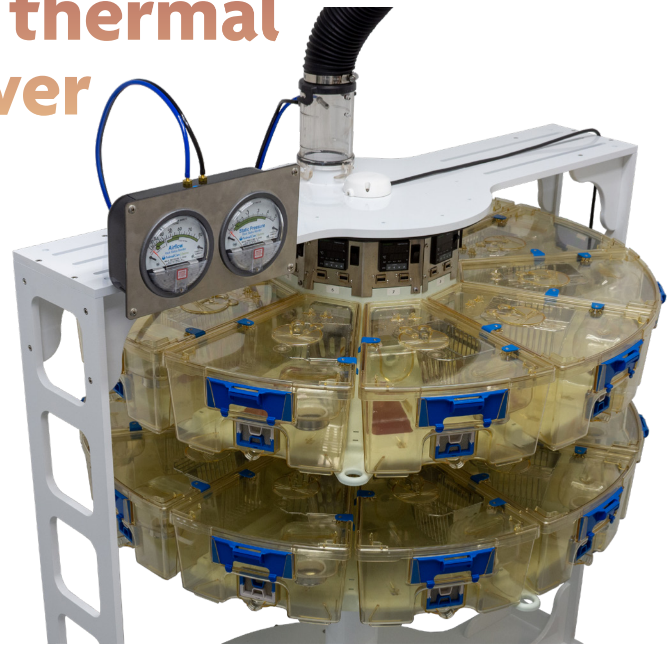

Figure 1. Optimice SMART system (Animal Care Systems, Centennial, CO).

INTRODUCTION: Laboratory rodents are typically housed in rooms set at temperatures between 20-22°C, primarily to match the comfort requirements of the humans working in these rooms. These temperatures are well below the rodent thermoneutral zone of 30-32°C[1], temperatures at which rodents maintain their body temperature without expending extra energy to keep warm. Housing rodents in temperatures lower than this thermoneutral zone subjects them to cold stress, which leads to changes in physiology, behavior, and immune function[2]. In addition, the core temperatures of anesthetized animals drop markedly; therefore, thermal support is critical to the successful recovery of rodents from anesthesia and surgery. The Optimice® SMART system is a 20-cage individually ventilated rack, with an individual heated disk provided to 10 cages. Although designed to counteract cold-stressed mice in the vivarium, we investigated whether this system can also be used for thermal support during recovery from anesthesia.

METHODS: Mice were recovered on either an electric heat blanket (MAXHeat, Kaz Inc., Southborough, MA) or the Optimice SMART system (Figure 1; Animal Care Systems, Centennial, CO); age, weight and sex were matched as closely as possible between these two test conditions. Mice were weighed and injected with 200 mg/kg propofol intraperitoneally. Seven out of the 11 mice tested received a subcutaneous transponder implanted via a large-bore needle under the skin (for an unrelated project; Figure 2) (4 mice in the heat blanket group, 3 in the SMART group, the remaining 4 mice did not receive any procedure; see Table 1). Mice were then placed back into the induction cage and once the body temperature fell below 35.7°C, placed in an Optimice cage on either the heat blanket (n=6) or in the SMART cage (n=5). Rectal temperature was measured with a Microtherma 2 Type T Thermocouple meter (ThermoWorks, American Fork, UT); mice were gently restrained by the tail and the probe was inserted into the rectum. Cage floor temperature was measured with a 905-T2 Surface Thermometer with Type K Sprung Thermocouple (Testo, West Chester, PA), placed directly on the cage floor over the central heat element of the heat blanket or the center of the heat plate (marked with an x) in SMART. Both rectal and cage floor temperatures were measured at least every 10-15 minutes. Other parameters such as sedation level, recumbency and activity/alertness/ambulation were also noted. Once rectal temperatures reached 36.5°C (normal rodent range 36.5-38°C) or above, the mouse was placed back into his/her home cage.

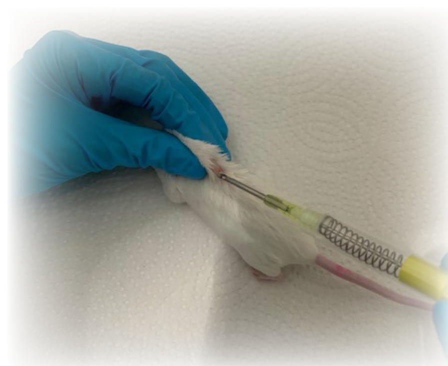

Figure 2. Subcutaneous transponder implantation.

The Optimice SMART heat plate occupies less than ¼ of the total cage floor surface area (Figure 3). Cages tested on the electric heat blanket were positioned so the heat

	Heat Blanket	SMART System
SQ Transponder	4	3
No Transponder	2	2
Total number	6	5

Table 1. Number of animals with and without a procedure for both test conditions.

Figure 3. The SMART heat plate (red disk) occupies the left back quarter of the cage.

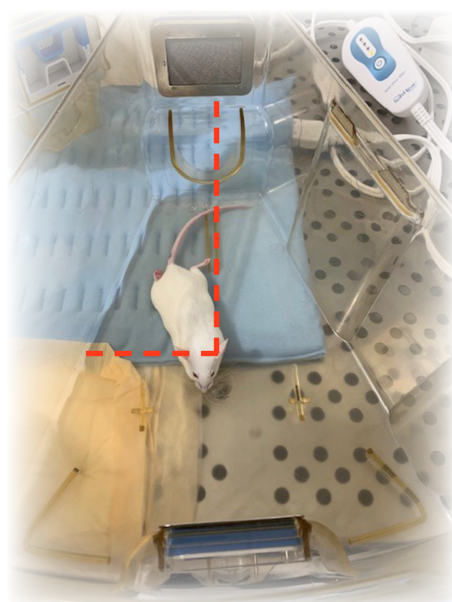

Figure 4. Heat elements of the electric heat blanket were positioned under the cage to occupy a similar configuration as the heat disk in the SMART system.

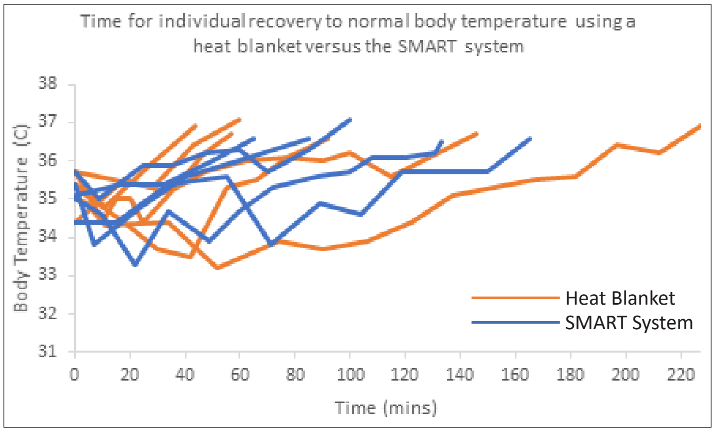

Figure 5. Rectal temperatures during recovery in heated cage until return to normal body temperature of at least 36.5°C (n=6 on heat blanket, lowest setting; n=5 in SMART system, heat plate set to 37-38°C). Return to normal body temperature ranged from 44 to 227 minutes.

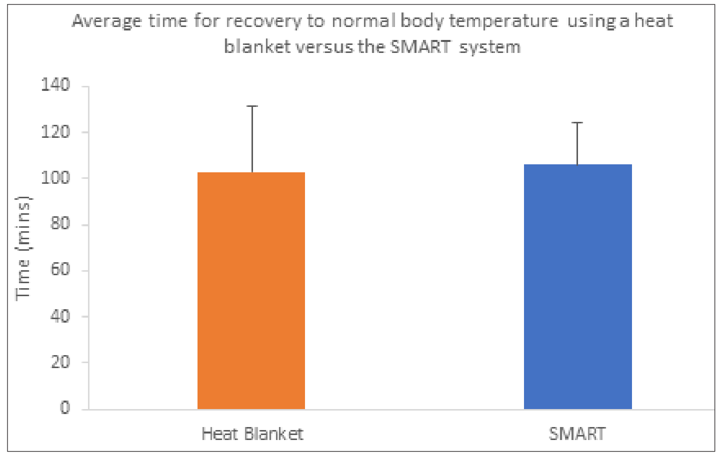

Figure 6. The average time for return to normal body temperature was comparable in both groups tested; 103 mins ± 28 (SEM) for the heat blanket versus 106 mins ± 18 (SEM) for SMART; t-test, P>0.05.

elements in the blanket occupied also approximately ¼ of the cage floor (Figure 4). The SMART heat element was set at 37-38°C and the heat blanket at the lowest setting.

Cage floor temperature averaged 33.4°C ± 0.2 (SEM) and 33.4°C ± 0.1 (SEM) for the heat blanket and SMART, respectively. Average time from injection to placement in either heated cage was similar (13 mins for the heat blanket and 14 mins for SMART). Body weight averaged 48.3 g ± 4.8 (SEM) for the heat blanket and 50.4 g ± 4.1 (SEM) for the SMART group; weights ranged from 36 - 68 grams.

RESULTS: Many of the mice did not become fully anesthetized (unconscious) but they did become sedate and recumbent, and their body temperatures fell well below normal range. The lighter mice appeared more heavily sedated upon injection and took on average more time to return to normal body temperature. All mice were alert and ambulatory, and exhibited grooming behavior considerably sooner than when their body temperature returned to normal; therefore, we used time to return to normal body temperature as the experimental endpoint (Figure 5).

The average time for recovery to normal body temperature was comparable between groups. Mean ± SEM = 103 ± 28 mins and 106 ± 18 mins for the heat blanket and SMART, respectively (t-test, P>0.05; see Figure 6).

DISCUSSION: General anesthesia affects several body systems, including thermoregulation. Decreased body temperature during anesthesia has potential negative effects, including delayed recovery to consciousness. Thermal support devices for small mammals are numerous (examples include water-circulating blankets, electric heat pads, microwaveable or thermogenic gel packs, heat lamps, forced air systems, etc.); however, these often require direct supervision, can be large and cumbersome and can occupy significant bench-top workspace. Some of these devices can also cause thermal burns, have auto-shutoff settings, may not provide cooler microclimates to allow mice to escape heat, and can be a fire hazard if left unattended for prolonged periods of time. Given these limitations, the SMART system was investigated as a safe, reliable and convenient alternative for thermal support during recovery from anesthesia. The current study demonstrated that recovery in the SMART system was equivalent to using an electric heat blanket, a commonly used thermal support device in laboratories to recover mice. However, recovering post-anesthetized mice in the compact SMART system has added benefits: it allows temperature control of individual cages and allows recovery in the home cage and room environment.

Providing thermal support to a cage of mice in its home rack location is difficult and impractical and consequently thermal support is usually provided only until sternal recumbency. However, Beale et al. confirmed that alterations in body temperature continue after the immediate postoperative period of thermal support; therefore, providing an external heat source for a prolonged time may benefit surgical recovery and overall success[3]. It may be beneficial therefore to utilize the SMART system for prolonged thermal support for rodents, not only during the first several hours after surgery but also long after their return to regular housing. Heat levels can be tailored to meet the thermal and physiological demands of individual cages and animals, the heat delivered is constant, can be supplied overnight, will not switch off or overheat, and does not present as a fire hazard. Additionally, it provides opportunity for mice to choose the heated floor area or a cooler surface in the cage. The latter advantage is equally important since mice also rapidly absorb heat, and it is essential to ensure mice do not overheat and become injured due to thermal supportive devices[4]. Further studies are being undertaken to study additional benefits of SMART for cold-stressed mice, certain experimental disease states, and breeding performance in laboratory animal environments.

REFERENCES:

1. Gordon, CJ. 2012. Thermal physiology of laboratory mice: defining thermoneutrality. J. Therm. Biol. 37:654–685.
2. Gaskill BN, Garner JP. 2017. Stressed out: providing laboratory animals with behavioral control to reduce the physiological effects of stress. Nature: Intl. J. of Sci. 46(4):142-145.
3. Beale CN, Esmail MY, Aguiar AM, Coughlin L, Merley AL, Alarcon Falconi TM, Perkins SE. 2018. Use of Air-activated Thermal Devices during Recovery after Surgery in Mice. JAALAS 57(4):392-400.
4. Baran S, Flegal M, Johnson E, Perret-Gentil M. [Internet]. 2012. Intraoperative physiological monitoring in rodent surgical research. [Cited Sept 2019]. Available at: https://www.laboratoryequipment.com/article/2012/10/intraoperative-physiological-monitoring-rodent-surgical-research

Acknowledgements: The authors would like to thank A. Corell, J. Tinaglia, J. Johannes and T. McKernan for help with editing, technical assistance and photos.

Team at Animal Care Systems in Centennial, CO: Bev Chua is the Staff Veterinarian and Dave Heldt is the Innovative Design and New Product Manager.