

THE DOUBLE SENSOR - A NON-INVASIVE DEVICE TO CONTINUOUSLY MONITOR CORE TEMPERATURE IN HUMANS ON EARTH AND IN SPACE

H.-C. Gunga^{1*}, A. Werner¹, A. Stahn¹, M. Steinach¹, T. Schlabs¹, E. Koralewski¹, D. Kunz³, D. L. Belavy⁴, D. Felsenberg⁴, F. Sattler², J. Koch²

¹*Department of Physiology, Center of Space Medicine, Charité Campus Benjamin Franklin, Berlin, Germany*

²*Draegerwerk AG & Co. KGaA, Luebeck, Germany*

³*Sleep research and Chronobiology, Department of Physiology, Center of Space Medicine, Charité Campus Benjamin Franklin, Berlin, Germany*

⁴*Centre of Muscle and Bone Research, Charité Campus Benjamin Franklin, Germany*

Contact person: hanns-christian.gunga@charite.de

INTRODUCTION

Under microgravity conditions astronauts/cosmonauts can experience substantial thermal discomfort, especially during extravehicular activities (Nicogossian et al. 1994). Since gravity is the driving force of convective heat transfer, even in highly thermally controlled space stations thermoregulation can be impaired and induce thermal discomfort. In turn, both physical and cognitive functioning can be negatively affected. Furthermore, continuous measurements of core body temperature would also promote fast and straightforward assessment of circadian rhythm, as core body temperature is tightly regulated by the suprachiasmatic nucleus. Given that it has been suggested that astronauts and cosmonauts might also suffer from desynchronization of the circadian system, monitoring of the circadian rhythm is crucial for promoting performance and health during space missions. Hence, a straightforward global indicator to continuously determine core body temperature in astronauts/cosmonauts would be very useful for monitoring health and improving physical and cognitive performance.

Very recently, we therefore presented a new method called Double Sensor, combining a skin surface temperature sensor with a heat flux sensor, to achieve this goal under various physical and environmental conditions (Gunga et al., 2005; 2008; 2009). Based on this experience we decided to use the Double Sensor during long-term bed-rest to establish whether rectal temperature recordings in humans could be replaced by a non-invasive skin temperature sensor combined with a heat flux sensor (Double Sensor) located at the forehead to monitor circadian core body temperature changes. This technology would be particularly useful for exploring changes in circadian rhythm during long-term micro-g exposure and was therefore evaluated as part of the 2nd Berlin BedRest Study (BBR2-2) in 2007/2008.

METHODS

Data collection of the present validation study was limited to the control group of the BBR2-2 (no training intervention). Rectal and Double Sensor temperature recordings were obtained for a

period of 36 h during 6-degree head-down tilt bed-rest. In order to analyse circadian rhythms for a period of 24 h, data were extracted at consecutive 30-min intervals between 19:30 h and 19:00 h the following evening. Based on an inclusion-threshold of 90% of data availability for a 24-h period, complete data were obtained for a total sample of seven subjects. All procedures were approved by the ethics committee of the Charité University Hospital Berlin and each participant gave their written consent after all procedures had explained to them.

Rectal temperature (T_{REC}) was recorded at a depth of 50 mm past the anal sphincter using 4-mm NTC-thermal sensors (YSI 400 compatible, BlueTemp® products, bluepoint medical GmbH & Co. KG, Selmsdorf, Germany). Data were collected at a frequency of 2 Hz, stored into flash memory systems (data logger, Heally-Sat Koralewski Industrie Elektronik, Hambühren, Germany), and subsequently transferred to a personal computer.

Temperature recordings employing the Double Sensor (T_{DS}) were performed at the forehead on the vertical line above the eye directly underneath the hairline. Details of the underlying biophysical model are given in Gunga et al. (2008). In contrast to similar methodological attempts in the past (Smith et al., 1980; Taylor et al., 1998), the heat flux sensor principle of the Double Sensor (Patent Draegerwerk No. DE 100 38 247, DE 101 39 705, 2003) has been miniaturized and used without extra heating, and has been specially sealed.

Data collection and handling were performed in accordance with rectal temperature processing. All statistical analyses were performed using the SPSS software (Version 16.00, SPSS Inc., Chicago, Illinois, USA). Measurements > 38.5 °C and < 36.0 °C were considered as artefacts and deleted from further analysis. Additionally, the remaining data was examined for outliers by identifying cases more distant than > 1.5 interquartil ranges from the 75th and 25th quartile. Agreement between methods was assessed by concordance correlation coefficients (CCC) and Bland-Altman plots. Limits within ± 0.5 °C were defined *a priori* as clinically acceptable. Cosinor analysis was performed within subjects for each temperature sensor to quantify circadian rhythm. Wilcoxon signed rank tests were employed to test fitting parameters and goodness-of-fit indices between the two temperature recoding techniques for significant differences. Finally, bias and limits of agreement were reported for the fitted cosine curve parameters to compare the random error component between methods.

RESULTS

Subject characteristics ($n = 7$) are given in Table 1.

Table 1 Descriptive subject characteristics (means \pm SD).

Age (years)	Height (m)	Body mass (kg)	BMI (kg/m ²)	T_{REC} (°C)	T_{DS} (°C)
31.9 \pm 8.0	1.79 \pm 0.04	80.8 \pm 5.6	25.3 \pm 2.0	36.82 \pm 0.37	36.91 \pm 0.45*

T_R , rectal temperature; T_{DS} , Double Sensor temperature; * Significantly different from from T_{REC} ($P < 0.001$).

Temperature recordings from the Double Sensor were moderately related to rectal temperature measurements ($r = 0.704$, $P < 0.001$). The corresponding scatter plot is given in Fig. 1 A. A number of data points ($n = 19$) exceeding the lower 95% confidence interval deserved closer inspection (grey-shaded data points). It was found that this scatter was predominantly caused by single subject during the interval between 23:30 h and 09:00 h. Given the better association for the subject's remaining data, it can be speculated that the rectal probe might not have been

correctly fixed in its original position. Deleting the data cloud increased the correlation coefficient to $r = 0.803$; $P < 0.001$). Similar findings were observed for CCC, which increased from its initial level of 0.678 to 0.773.

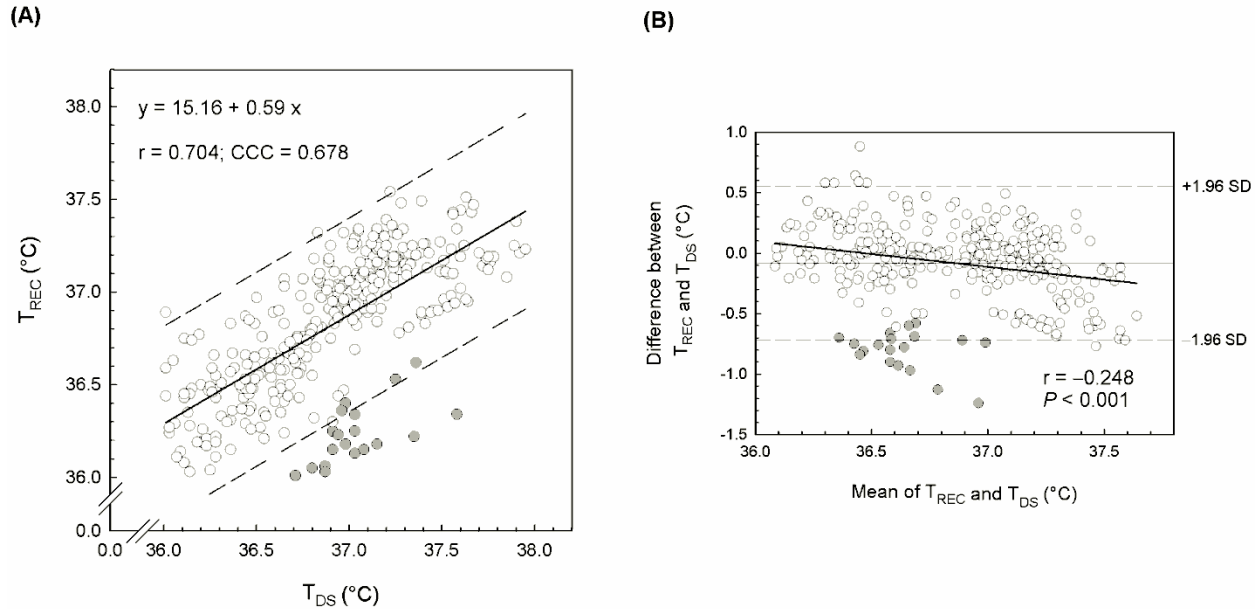


Fig. 1 (A) Scatter plot of rectal and Double Sensor temperature recordings. T_{REC} , rectal temperature. T_{DS} , Double Sensor temperature. (B) Bland-Altman plot of the difference between the methods against the mean of methods. T_{REC} , rectal temperature. T_{DS} , Double Sensor temperature. The solid line indicates the bias between methods and dashed lines are 95% limits of agreement (± 1.96 SD). Proportional error is indicated by a significant relationship between differences and means of methods. Extreme values are grey-shaded. Reported statistics are based on all data shown (Gunga et al. 2009).

Agreement between methods is indicated in Fig. 1 B. There was a slight (0.08 ± 0.32 °C), but significant difference between T_{REC} and T_{DS} ($P < 0.001$). 95% of the differences were located between -0.72 °C and $+0.55$ °C. Omission of the apparent extreme values indicated above, 90% of the data were within limits of ± 0.5 °C, and 73% within limits of ± 0.25 °C.

Visual inspection revealed that the Double Sensor underestimated rectal temperature at lower temperatures and overestimated rectal temperature at higher temperatures. This proportional error was also confirmed by linear regression analysis ($r = -0.248$, $P < 0.001$). Recalculation of the limits of agreement after data deletion of the apparent artefacts (grey-shaded data points) according to Fig. 1 A reduced the upper bound to $+0.49$ °C and the lower bound to -0.57 °C. Graphical inspection of time series data for each individual subject revealed distinctive circadian patterns. This rhythm was confirmed by cosinor analysis as amplitudes were significantly different from 0 for all subjects ($P < 0.001$). Fig. 2 shows cosinor analysis for an individual subject for both rectal and Double Sensor recordings.

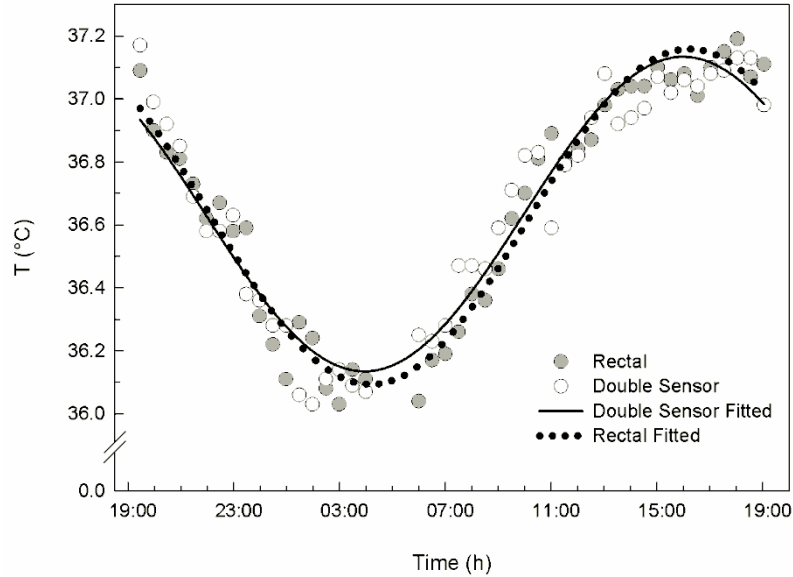


Fig. 2 Scatter plot and regression lines obtained from cosinor analysis for rectal (black dots, dotted line) and Double Sensor (white dots, solid line) temperature data as a function of time from a single subject (Gunga et al. 2009).

The high degree of visual agreement between measurements indicated in Fig. 2 was also confirmed by parameters of the fitted cosine curves ($y(t) = 36.63 + 0.53 \cos(t + 20.68)$; $R = 0.979$ and $y(t) = 36.63 + 0.50 \cos(t + 20.46)$; $R = 0.962$ for rectal and Double Sensor data, respectively). This finding was also observed in the total group. Comparison of curve characteristics between rectal and Double Sensor recordings for the total group is given in Table 2. When circadian temperature profiles were quantified by mesor, acrophase, and amplitude, no significant difference were found between rectal and Double Sensor temperature recordings ($P = 0.310$ to 0.866).

Table 2 Cosinor analysis for rectal and Double Sensor temperature recordings (mean \pm SD).

	Rectal	Double Sensor	Bias	LoA ^a	<i>P</i>
Mesor (°C)	36.79 \pm 0.13	36.90 \pm 0.24	-0.11	-0.67 to 0.45	0.310
Acrophase (rad)	5.55 \pm 0.21	5.51 \pm 0.22	0.04	-0.31 to 0.39	0.735
Amplitude (°C)	0.48 \pm 0.07	0.49 \pm 0.08	-0.01	-0.21 to 0.19	0.866

^a LoA, limits of agreement (bias \pm 1.96 SD).

Further information about the degree of agreement between methods is provided by the limits of agreement. Of particular interest is the random error component for acrophase and amplitude. As indicated in Table 2, individual differences for amplitude range between -0.21 °C and 0.19 °C. More importantly, differences in acrophase were as low as about 1 h (1.18 h to 1.49 h). Finally, it should be noted though that Double Sensor recordings were characterized by higher variation compared to rectal temperature measurements, yielding a poorer model fit. This was also statistically confirmed by a significantly greater amount of total variance accounted for by the rectal cosine curve model (0.93 vs. 0.79, $P < 0.05$) and significantly lower residual summed squares (0.48 vs. 1.69, $P < 0.05$) compared to the Double Sensor fitted cosine curve.

CONCLUSIONS

Given the number of drawbacks of present technological advances for monitoring core body temperature – under rest and exercise – there is a great demand for developing an easy-to-operate and non-invasive technology to measure core body temperature in humans. In the present study we evaluated a new skin temperature and heat flux measurement device, called the Double Sensor to monitor core body temperature changes during 24 h 6°-head-down tilt bed-rest. Though 95% of individual differences between the methods ranged between -0.72 °C and $+0.55$ °C, it should be noted that 85% (i.e. 90% after omission of apparent extreme values) of the differences were located within the *a priori* defined limits of ± 0.5 °C. In this regard it seems noteworthy that rectal temperature recordings themselves are not without error. Furthermore, it was found that circadian core temperature profiles could be well approximated by the Double Sensor. These results confirm the findings from our previous study where we validated the Double Sensor during treadmill exercise (Gunga et al., 2008) with limits of agreement ranging between -0.90 °C and $+1.06$ °C. Furthermore, there were no significant mean differences for cosine curve fitted parameters ($P = 0.310$ to 0.866) and differences in amplitude and acrophase for an individual were as low as about 0.2 °C and 1 h, respectively. Thus, in spite of relative marked variability for single ‘spot checks’, we therefore suggest that the Double Sensor placed at the forehead seems to be a valuable approach for monitoring 24-h core body temperature changes (circadian rhythm) during long-term 6°-head-down tilt bed-rest.

In conclusion, the knowledge and technological development gained from the study could promote applications of continuous core body temperature measurements in clinical, occupational, sports and environmental medicine on earth and in space. The Double Sensor device might be an effective, non-invasive and easy-to-operate technology to gain fundamental insights into cardio-circulatory regulation, thermoregulation, and circadian rhythms in humans and we suggest further studies to fully reveal the underlying potential of the technique by improving its technology and testing it in various subject cohorts and diverse settings under different conditions.

REFERENCES

- Gunga, H.-C., Sandsund, M., Reinertsen, R.E., Sattler, F., Koch, J., 2005. The "Double sensor" - A new non-invasive device to measure continuously core temperature in humans. In: Environmental Ergonomics XI, Holmér, I., Kuklane, K., Gao, C. (eds.). Proceedings from the 11th International Conference on Environmental Ergonomics, 286–289. Ystad, Sweden.
- Gunga, H.-C., Sandsund, M., Reinertsen, R.E., Sattler, F., Koch, J., 2008. A non-invasive device to continuously determine heat strain in humans. *J. Therm. Bio.* 33, 297–307.
- Gunga, H.C., Werner, A., Stahn, A., Steinach, M., Schlabs, T., Koralewski, E., Kunz, D., Belavý, D. L., Felsenberg, D., Sattler, F., Koch, J., 2009. The Double Sensor - A non-invasive device to continuously monitor core temperature in humans on earth and in space. *Respiratory Physiology & Neurobiology*. In Press. DOI: 10.1016/j.resp.2009.04.005
- Nicogossian, A.E., Leach Huntoon, C., Pool, S.L., 1994. *Space physiology and medicine*. 3rd ed. Philadelphia: Lea & Fibiger.
- Smith, P., Davies, G., Christie, M.J., 1980. Continuous field monitoring of deep body temperature from the skin surface using subject-borne portable equipment: some preliminary observations. *Ergonomics* 23(1), 85–86.
- Taylor, N., Wilshire, B., Amos, D., Takken, T., Komen, T., Cotter, J.D., Jenkins, A., 1998. Indirect measurement of core temperature during work: Clothing and environmental influences. Abstracts of the 8th International Conference on Environmental Ergonomics 97, San Diego, CA, USA.