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Calibration of an ingestible temperature sensor

A P Hunt and I B Stewart

Institute of Health and Biomedical Innovation and School of Human Movement Studies, Queensland University of Technology, 60 Musk Avenue, Kelvin Grove, QLD 4059, Australia

E-mail: ap.hunt@qut.edu.au

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Abstract
An ingestible telemetric sensor for measuring core body temperature is increasingly being utilized in occupational and athletic studies of heat strain. There is a need for a uniform method of calibrating these sensors in the scientific community in order to effectively compare the results of different researchers. The purpose of the present investigation was to determine and present such a calibration procedure. Sensors were placed in a water bath heated to nine discrete temperatures, and the recorded values were compared to that of a traceable thermometer. It was observed that sensor 2 recorded temperatures higher than sensors 1 and 3, and that all sensors were higher than the traceable thermometer, highlighting the need for a calibration procedure. The findings of this study suggest a number of recommendations for a calibration procedure including: (1) four water bath temperatures in the range of 33–41 ºC should be utilized; (2) sensors should be immersed for a minimum of 4 min prior to taking a measurement; (3) a linear regression relating sensor temperature to a traceable thermometer is an appropriate method to adjust raw data. Switching the sensor off after calibration and reactivating it prior to ingestion will not influence the accuracy of temperature measurement.

Keywords: core body temperature, calibration, ingestible temperature sensor

(Some figures in this article are in colour only in the electronic version)
the individual to developing heat illness. For such minute elevations in core body temperature to have significant implications for health and safety indicates the need for a high degree of accuracy in the measurement of core body temperature.

Core body temperature has traditionally been measured in the esophagus or rectum to obtain the most accurate and reliable readings. However, these methods are limited to laboratory research due to safety concerns and the restrictions to movement they impose. In a clinical setting, core body temperature is commonly measured at the tympanic membrane through the use of infrared ear thermometers. However, the temperature reading may be influenced by factors such as the emissivity of the surface measured, exercise and a warm or cold environment, and it is recommended that more reliable methods should be used for accurate temperature reading (Pusnik et al. 2004). A relatively new device to measure core body temperature consists of an ingestible sensor, which has a silicone coating encapsulating a telemetry system and a quartz crystal temperature sensor. The sensor vibrates at a frequency related to the surrounding temperature and produces a low-frequency signal that is picked up by a recorder located on the person’s waist. The recorder is light weight, compact and does not restrict normal movement patterns, and therefore allows the monitoring of core (intestinal) temperature during normal daily activities. With this advantage in mind, many researchers are finding the telemetric system a useful tool to measure heat strain in both athletic and occupational settings (Brake and Bates 2002, Byrne et al. 2006, Edwards and Clark 2006, Laursen et al. 2006).

Several studies comparing intestinal temperature to esophageal or rectal temperature (or both) have shown good agreement between the methods (Easton et al. 2007, Gant et al. 2006, Lee et al. 2000, O’Brien et al. 1998). A recent review of these and other papers has shown that intestinal temperature has a systematic bias <0.1 °C and 95% limits of agreement (LoA) within ± 0.4 °C compared to esophageal temperature. Intestinal temperature compared to rectal temperature also has LoA within this range, although a systematic bias >0.1 °C is commonly found. It was concluded that intestinal temperature measured by an ingestible sensor is a valid measure of core body temperature (Byrne and Lim 2007). However, to achieve this level of accuracy Byrne and Lim (2007) note that individual sensors should be calibrated against a certified thermometer prior to ingestion.

The reason for suggesting that the ingestible sensors should be calibrated comes from several studies that have assessed the temperature of a water bath. Sparling et al. (1993) placed six sensors in a water bath of 40 °C and monitored temperature decline to 35 °C. Across this temperature range three sensors measured temperature higher (0.25–0.6 °C) and three lower (0.05–0.10 °C) than a certified thermometer. Lee et al. (2000) heated a water bath to 30, 34, 38 and 42 °C, and reported sensor temperature to be significantly lower than a certified thermometer, although the magnitude of this difference was not stated. At a single water bath temperature of 39.0 ± 0.01 °C, Wilkinson et al. (2008) found sensor temperature to average 39.06 ± 0.02 °C, with a range of 0.08 °C. These observations show that each sensor has a bias from temperature measured by a certified thermometer and that the magnitude of this bias varies between different sensors. As each sensor is ‘one use only’, calibrating all sensors to a standard device will allow for comparing core body temperature measured by different sensors.

Currently, there is no consensus on the best approach for sensor calibration. Several studies utilizing the ingestible sensor do not report any calibration procedures (Kolka et al. 1993, Edwards et al. 2002, Niess et al. 2003, Brake and Bates 2002, Laursen et al. 2006). Another study reports that a calibration was performed, but does not specify how it was conducted (Gant et al. 2006). A number of researchers report measuring a range of water bath temperatures for calibration purposes. Water bath temperatures between 35 and 43 °C have
been used to check that sensor accuracy was ±0.1 °C, however these authors do not report correcting raw data subsequently collected (Byrne et al 2006, Wilkinson et al 2008). Others report that if sensors were found to be inaccurate, then they were discarded (Easton et al 2007, Kolka et al 1997). However, an attempt was made to change the calibration number using a proprietary formula prior to discarding sensors (Easton et al 2007). Finally, some researchers have utilized the findings of water bath temperatures between 30 and 42 °C, measured by both the ingestible sensor and a certified thermometer, to correct raw data from subsequent testing of core body temperature. Sparling et al (1993) do not elaborate on how this correction was performed. O’Brien et al (1998) note that a linear regression relating sensor frequency to temperature was developed from three water bath temperatures (33, 37 and 41 °C), and used to adjust raw frequency data. Alternatively, Lee et al (2000) and Edwards and Clark (2006) report correcting raw data by a linear calibration curve relating temperature recorded from the ingestible sensor and a certified thermometer at four water bath temperatures (30, 34, 38 and 42 °C).

Overall, a wide range of methods to ensure the accuracy of ingestible sensor measurement has been implemented in the scientific community. In order for effective comparisons to be made between studies, a uniform procedure for calibrating ingestible temperature sensors should be adopted. Therefore, the aim of this investigation is to determine and present an accurate calibration procedure for ingestible temperature sensors.

2. Methods

2.1. Experimental procedures

A water bath was heated to nine discrete temperatures (~23, 28, 33, 35, 37, 39, 41, 46 and 51 °C). A traceable thermometer (TL-1W, ThermoProbe, Jackson MS, USA) with a reported accuracy of ±0.06 °C was used as the standard measure of water bath temperature. Temperature was allowed to stabilize at each increment prior to immersing an ingestible temperature sensor (CorTemp, HQinc, Palmetto FL, USA) in the water bath. Upon immersion, sensor temperature was recorded every 10 s for 6 min. This allowed for the determination of the time required for the sensor to reach a stable temperature. The average temperature over the final minute of immersion was taken as the sensor temperature and used for comparison to the TL-1W. This process was repeated for all water bath temperatures within one day. The time between temperature measurements ranged between 30 and 60 min, during which time the sensor remained at room temperature. All temperatures were then reassessed on two subsequent days. The sensor was left active between day 1 and 2 to assess if the temperature reading would vary with battery life. Between day 2 and 3, a magnet was placed next to the sensor, switching it off. Removing the magnet prior to testing on day 3 reactivated the sensor. This was to assess if the accuracy of the sensor changed if it was turned off and on. A total of three different sensors were tested.

2.2. Statistical analysis

The time required for sensor temperature to equilibrate with water temperature was assessed by plotting the consecutive 10 s change in temperature over the 6 min of immersion. A change of less than 0.05 °C from one reading to the next observed consistently was taken to indicate equilibration. To assess the level of agreement between the two devices, the difference score (ingestible sensor—TL-1W) was calculated. The mean difference score across the nine water bath temperatures was calculated to assess for a systematic bias between the devices. This
was done for all days of testing for each sensor. Bland–Altman plots of the difference score compared to the mean of the two devices were constructed. Acceptable agreement between devices was set as a systematic bias of <0.1 °C and 95% limits of agreement ±0.4 °C. A univariate analysis of variance was used to assess for the effects of sensor and day on the mean difference score. Statistical software (SPSS version 15.0) was used. Least-squares regression was used to determine the linear relationship between the ingestible sensor and TL-1W devices. A significance level of $p < 0.05$ was chosen.

From the data gathered here, it is the goal to determine the minimum number of data points required to develop a linear calibration curve. The formula for calculating standard error was re-written to determine the required number of data points:

$$\text{N} = \frac{\text{SD}^2}{\text{SE}^2}$$

(1)

where SE is the standard error, SD is the standard deviation, and $\text{N}$ is the sample size. The standard deviation was obtained as the square root of the mean-square-error term for the residual of the univariate ANOVA. The standard error was set at 0.033. This value was chosen as the known accuracy of the ingestible sensor device is ±0.1 °C; thus, the measured temperature should range between $-0.1$ and $+0.1$ °C of the actual temperature. For a normal distribution, this range can be split into six parts, representing the standard deviation. A range of 0.2 divided by 6 equals 0.033. Therefore, this is the largest acceptable standard error.

3. Results

Figure 1 displays the change in temperature between consecutive values recorded by the ingestible sensor over 6 min for each water bath temperature. It can be seen that as time progresses, the change in temperature from one reading to the next approaches zero, indicating a stable value. The time required to attain the criteria of a less than 0.05 °C change between readings tended to increase with water bath temperature. However, for all bath temperatures, between 3 and 4 min of water immersion was required for the consecutive 10 s change to be minimal, and it remained stable after this point. This observation was consistent between the sensors and across the days of testing.

Table 1 presents the mean difference score and measures of variance between the ingestible sensors and TL-1W devices for all three sensors across the three days of testing. For sensors 1 and 3 the mean difference and limits of agreement were consistently within the specified range of <0.1 °C and ±0.4 °C. Sensor 2 also falls within the required limits of agreement; however, the systematic bias was greater than 0.1 °C. A representative Bland–Altman plot of the results presented in Table 1 can be observed in figure 2. An interesting observation is that error in temperature reading from the ingestible sensor appears to increase with temperatures at the extremes of the range studied. However, error is least in the physiological range of ~33–41 °C.

Univariate analysis of variance revealed no main effect for day ($F = 0.036, p = 0.965$), and no interaction between day and sensor ($F = 0.018, p = 0.999$). However, a significant main effect for sensor was observed ($F = 10.818, p < 0.001$). Pairwise comparisons with Bonferroni adjustment for multiple comparisons revealed that the temperature difference between the ingestible sensor and the TL-1W was greater for sensor 2 compared to sensor 1 ($p = 0.003$) and sensor 3 ($p < 0.001$). The mean-square-error term of the residual in the univariate ANOVA was 0.004, equalling a standard deviation for the difference score of all pill measurements to be 0.063. Using this standard deviation in equation (1) with a standard error of 0.033 yielded an $\text{N}$ of 3.67.
Figure 1. Consecutive 10 s change in temperature measured by sensor 1 on day 2 over 6 min water immersion for all nine water bath temperatures. Solid lines indicate ±0.05 °C requirement for stabilization; dashed lines show the elapsed time at 3 and 4 min.

Table 1. Mean difference and measures of variation for the three temperature sensors across three days of testing in comparison to the TL-1W.

<table>
<thead>
<tr>
<th>Sensor 1</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean difference (°C)</td>
<td>SD a</td>
<td>SE b</td>
<td>Upper CF c</td>
</tr>
<tr>
<td>Day 1</td>
<td>0.09</td>
<td>0.06</td>
<td>0.02</td>
</tr>
<tr>
<td>Day 2</td>
<td>0.08</td>
<td>0.05</td>
<td>0.02</td>
</tr>
<tr>
<td>Day 3</td>
<td>0.08</td>
<td>0.05</td>
<td>0.02</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sensor 2</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean difference (°C)</td>
<td>SD a</td>
<td>SE b</td>
<td>Upper CF c</td>
</tr>
<tr>
<td>Day 1</td>
<td>0.15</td>
<td>0.08</td>
<td>0.03</td>
</tr>
<tr>
<td>Day 2</td>
<td>0.15</td>
<td>0.07</td>
<td>0.02</td>
</tr>
<tr>
<td>Day 3</td>
<td>0.14</td>
<td>0.08</td>
<td>0.03</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sensor 3</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean difference (°C)</td>
<td>SD a</td>
<td>SE b</td>
<td>Upper CF c</td>
</tr>
<tr>
<td>Day 1</td>
<td>0.07</td>
<td>0.06</td>
<td>0.02</td>
</tr>
<tr>
<td>Day 2</td>
<td>0.07</td>
<td>0.05</td>
<td>0.02</td>
</tr>
<tr>
<td>Day 3</td>
<td>0.07</td>
<td>0.05</td>
<td>0.02</td>
</tr>
</tbody>
</table>

a SD: standard deviation of mean difference.
b SE: standard error of mean difference.
c CI: 95% confidence interval.
d LoA: 95% limits of agreement.

The relationship between the ingestible sensor and TL-1W temperature measurements in the physiological range was assessed via a linear regression (table 2). The relationship was found to be highly linear, with coefficients of determination ($r^2$) of 1.00, indicating that 100% of the error in one device could be predicted by the other.
Figure 2. Bland–Altman plot of the ingestible sensor and TL-1W across nine water bath temperatures for sensor 1 on day 3. Solid line indicates the mean difference; dashed lines represent the 95% limits of agreement.

Table 2. Slope, intercept and coefficient of determination for the linear regression of ingestible sensor and TL-1W data in the physiological range on day 1.

<table>
<thead>
<tr>
<th></th>
<th>Slope</th>
<th>Intercept</th>
<th>$r^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensor 1</td>
<td>1.0005</td>
<td>−0.0700</td>
<td>1.00</td>
</tr>
<tr>
<td>Sensor 2</td>
<td>1.0061</td>
<td>−0.3428</td>
<td>1.00</td>
</tr>
<tr>
<td>Sensor 3</td>
<td>1.0031</td>
<td>−0.1553</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* Only three data points used in regression.

4. Discussion

The present investigation has shown that at least 4 min of water immersion is required for the ingestible sensor to attain a stable reading of temperature. This finding has important implications for developing procedures to verify the calibration of the ingestible temperature sensors. It indicates that sensors will need to be immersed in water for a minimum of 4 min prior to taking a reading of temperature for comparison to a traceable thermometer. Previous researchers have only utilized a 2 min time period to achieve a stable reading (Lee et al. 2000). The current findings suggest that this length of time is insufficient to achieve stabilization, and would result in the development of an inaccurate calibration curve.

Each ingestible sensor showed a positive systematic bias, indicating that it consistently measured temperature higher (0.07–0.15 °C) than the TL-1W. Similar findings have been reported previously (Sparling et al. 1993, Wilkinson et al. 2008). In addition, the systematic bias differed between sensors, such that sensor 2 was outside the required accuracy range, whilst sensors 1 and 3 were within. These findings highlight the importance of establishing a method to verify the calibration of each sensor and correct raw data to that of a traceable
thermometer. Following such a procedure will allow for comparing differences between
individuals, and comparing the same individual on multiple occasions, requiring the use of
more than one sensor.

The ingestible sensor will remain in the gastrointestinal (GI) tract for \( \sim 30 \) h (Kolka et al
1993). In order to detect changes in core body temperature, it is important for measurement
accuracy to be consistent over this time period. The location of the sensor within the GI tract
also needs to be considered as temperatures in the stomach and upper GI tract are influenced
by food and fluid ingestion (Wilkinson et al 2008). For this reason, it is recommended
that recording sensor temperature commences at least 6 h after ingestion (Byrne and Lim
2007). The findings of the present investigation show that within each sensor the level of
accuracy remained constant across three days of testing. Therefore, subsequent research of
core temperature over extended periods can be confident that observed changes reflect actual
changes in temperature and not random error of measurement. Another conclusion that can
be drawn from this finding is that turning the sensor off (by placing it next to a magnet) does
not influence its accuracy upon reactivation. Since the sensor only has a limited battery life,
knowing that the sensor can be turned off following measurements for calibration, and before
ingestion has practical implications for the logistics of scientific studies utilizing the ingestible
sensors.

To eliminate the small systematic bias in the sensors it is recommended that a linear
calibration curve be applied to raw data. Bland–Altman plot analysis revealed that error
was least when temperature was measured in a range of \( \sim 33–41 \) °C, corresponding to
the temperature range found in the human body. The results of the present investigation
indicate that a minimum of four water bath temperatures should be assessed to establish an
accurate calibration curve. The current data allowed for the use of five data points to calculate
the calibration curve for sensors 2 and 3 on day 1, but only three data points were available
for sensor 1. The high coefficient of determination for these regressions (table 2) indicates
that estimation of the actual temperature from that measured by the ingestible sensor will be
highly accurate. Other studies have reported similarly high coefficients of 0.99 (Lee et al
2000, O’Brien et al 1998). Therefore, applying a linear regression to the data obtained in a
physiological range is a suitable method of calibration.

There are two points that should be taken into account when considering the wider
applicability of the conclusions drawn from this study. Firstly, only one model of sensor was
tested. Secondly, the time to attain a stable temperature reading will depend on the weight and
composition of the sensor itself, and this may also vary between different models of sensor.
The findings presented in this investigation may not generalize to sensors of differing models.

To summarize, ingestible temperature sensors show a small positive systematic bias to
that of a traceable thermometer. In addition, different sensors vary in the magnitude of that
bias. Therefore, a procedure to calibrate the sensor needs to be administered to enable the
comparison of core body temperature from different pills (in different individuals or the same
individual on multiple occasions). Such a calibration procedure has been developed in the
present investigation, and consists of three components. (1) A minimum of four water bath
temperatures in the physiological range of 33–41 °C should be assessed. (2) Sensors should
be allowed 4 min immersed in the water bath prior to taking a reading for comparison to a
traceable thermometer. (3) A linear regression relating these four temperatures can then be
used to adjust the subsequent raw data of that sensor. The present investigation also indicates
that turning the sensor off following calibration will not affect the accuracy of the sensor.
Conflict of interest statement

The authors declare that there are no conflicts of interest in this work.

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