Validity and reliability of the myTemp ingestible temperature capsule

ABSTRACT

Objectives. An accurate and non-invasive measurement of core body temperature (Tc) is of great importance to quantify exercise-induced increases in Tc in athletes or to assess changes in Tc in patient populations. The use of ingestible gastrointestinal telemetric temperature capsules is widely accepted as a surrogate marker for Tc, but widespread implementation is lacking due to the high costs of these disposable capsules. A new and cheaper temperature capsule system (i.e. myTemp) was recently introduced. The aim of present study is to determine the validity and test-retest reliability of the myTemp system.

Design. Ex-vivo experimental study.

Methods. Fifteen ingestible temperature capsules (myTemp, Nijmegen, Netherlands) were tested in a highly temperature controlled water bath, in which the water temperature gradually increased from 34°C to 44°C. The study protocol was performed twice for each temperature capsule.

Results. Mean difference between myTemp temperature and water bath temperature was -0.001±0.005°C (Limit of Agreement (LOA): ±0.011°C) during Trial 1 ($p=0.11$) and -0.001±0.006°C (LOA: ±0.012°C) during Trial 2 ($p=0.039$). Furthermore, an Intraclass Correlation Coefficient (ICC) of 1.00 was found for both trials. A systematic difference between Trial 1 and 2 of 0.004±0.008°C (LOA: ±0.015°C) was found ($p<0.001$), whereas the ICC between both trials was 1.00 and the standard error of measurement was 0.005°C.

Conclusion. Although we found a systematic bias for the sensitivity (-0.001°C) and reliability (0.004°C), these values can be considered insignificant from a physiological and clinical perspective. Thus, the myTemp ingestible temperature capsule is a valid technique to measure (water) temperature under controlled circumstances.

Key Words: Thermoregulation, thermometer, intestinal temperature, core body temperature

INTRODUCTION

Core body temperature (Tc) reflects the temperature of the abdominal, thoracic and cranial cavities of the body, which can be measured as an esophageal, pulmonary artery, intestinal and rectal temperature. In healthy individuals Tc is typically regulated between 36.2°C and 37.7°C[1, 2], with a continuous balance between heat production and heat loss[3]. Exercise induces a thermoregulatory burden, as only a minority (i.e. 1% - 20%) of the metabolically produced energy can be used as muscle power, whereas the majority (i.e. 80% - 100%) of the energy is released as heat[4-6]. The response of heat loss mechanisms to increased heat production during exercise is often delayed and insufficient, which results in heat accumulation and an increase in Tc, which reduces exercise performance and increases the risk to develop heat-related illnesses such as heat exhaustion and heat stroke during un-compensable heat stroke[7].

In order to protect individuals from severe heat-related illnesses it is important to monitor Tc and anticipate on high Tc levels. Unfortunately, measurement of Tc is difficult. Intra-Pulmonary arterial temperature is currently considered as the gold standard for Tc[8]. However, this Tc measurement is invasive and only applicable in clinical settings. Alternatively, athletes have been using ingestible temperature capsules to wirelessly measure gastrointestinal temperature as a valid surrogate marker of Tc[9-12]. Although several commercial systems are available, current temperature capsules and data recorders are expensive and have important restrictions such as battery lifetime and expiry. A Dutch start-up company, myTemp (www.myTemp.nl), developed and patented a novel ingestible telemetric temperature capsule system, which is cheaper and does not have a battery. However, the precision of this temperature system has not been investigated yet.

Therefore, the aim of present study is to determine the validity and test-retest reliability of the myTemp ingestible temperature capsule. We used an ex-vivo water bath for optimal control of testing conditions. We hypothesized that the myTemp temperature capsule is valid and reliable to measure Tc, with a systematic bias for both parameters <0.1°C.

METHODS

In this ex-vivo experimental study a total of n=15 myTemp ingestible temperature capsules were tested in a custom made highly controlled water bath. The primary outcomes were the validity and test-retest

reliability. Two measurements were performed per temperature capsule, using a similar study protocol. All measurements were conducted within a 48 hour period to prevent any drifting due to changes in environmental factors.

The myTemp system consists of an ingestible temperature capsule (8 x 20 mm in size, 1.3 g) and a copper-wired waistband which created a magnetic field (myTemp, Nijmegen, Netherlands). The ingestible capsule is activated by the magnetic energy of the waistband under the condition that capsule lies within the circle of the waistband and that the capsule and waistband are within a 30 cm range of each other. The capsule measures its surrounding temperature using a NTC thermistor and sends the data wirelessly to the waistband. Temperature is logged at predefined intervals, which was established at 6 seconds (10 measurements/minute) for the present study. Furthermore, the myTemp capsule is able to record temperature with a detection resolution of 0.01°C.

A thermostat-controlled and distilled water-filled bath (3.5 L) was used in which four highly sensitive wired temperature probes (Fluke Hart Scientific 1529 Chube E-4 Thermometer Readout, Everett, USA) measured temperature up to 0.002°C exactly. The average value of these wired temperature sensors represented the temperature of the water bath. In addition, a heater (Fluke Hart Scientific 2100 Temperature Controller, Everett, USA) and stirrer (Heidolph Instruments D91126, type RZR1, Schwabach, Germany) system ensured thermal homogeneity of the water bath. A custom made holder prevented the sensor reaching the bottom of the water bath or coming into contact with another sensor. The myTemp waistband was placed around the water bath with a distance range of 0.2 m from the ingestible temperature capsule. Moreover, the environment in which the equipment was located was also free of signal interference, which may be caused by electromagnetic fields such as computers or phones. An impression of the study setup is presented in Supplemental Figure 2.

During the measurement protocol the water temperature gradually increased from 34°C to 44°C, mimicking the physiological range between hypothermia (<35°C) and exertional hyperthermia (>40°C). An automated protocol was programmed to perform the stepwise increase in water temperature,

resulting in eleven plateaus (34, 35, 36, 37, 38, 39, 40, 41, 42, 43 and 44°C, Supplemental Figure 1). For each temperature plateau, three conditions had to be achieved before the protocol could proceed:

1) Water bath temperature did not vary >0.02°C during fifty consecutive measurements.
2) Water bath temperature did not vary >0.01°C during two consecutive measurements.
3) The change in heater power did not exceed 4% during two consecutive measurements.

These conditions ensured stability of the water bath temperature and thereby reliable temperature measurements at each point of measurement. The study protocol was performed twice for each temperature capsule (Trial 1 / Trial 2), which allowed us to calculate the validity and test-retest reliability.

The average of the last 25 temperature readings per temperature plateau was calculated and compared to the average water bath temperature over the same period. This resulted in 11 comparisons between the myTemp temperature system and water bath per ingestible temperature capsule. In order to establish the validity of the myTemp capsules, the Bland-Altman method for assessing the agreement between two methods was used[13]. In short, the mean difference between the myTemp temperature system and water bath was assessed using a one-sample T-test. The systematic bias and accompanying 95% Limits of Agreement (LOA) were derived from the Bland-Altman plot[13]. Furthermore, a bi-variate correlation plot was constructed for the average temperature of the myTemp capsules and the average water bath temperature. The Intraclass Correlation Coefficient (ICC) was calculated for the average of all 15 capsules, to determine the inter-measure agreement[14]. The Standard Error of Measurement (SEM) was calculated based on the standard deviation (SD) of the difference between myTemp and water bath temperature[15]. Furthermore, we conducted a Repeated Measures ANOVA to determine whether the accuracy of the myTemp capsule (defined as Δ water bath - myTemp temperature) was different across the physiological temperature range.

A similar approach was used to determine the test-retest reliability. A Bland-Altman plot was constructed to determine the agreement of the myTemp ingestible capsule data between the first and second measurement. Furthermore, a bi-variate correlation plot was created and the ICC for agreement

and 95% LOA were reported. The SEM was determined using the SD of the difference of myTemp temperature between Trial 1 and 2.

All statistical analyses were performed using SPSS Statistics (Version 20), in which the level of significance was set at $p<0.05$. The mean difference was reported as mean difference ± SD, unless indicated otherwise.

RESULTS

All tests were performed successfully and data was collected within 4 weeks. No signs of data interference were observed and no outliers were detected.

Validity. The mean difference between the myTemp temperature and the water bath temperature was -0.001±0.005°C during the validation Trial 1, and no evidence of a systematic bias was found ($p=0.11$) (Figure 1A). Furthermore, the LOA were ±0.011°C. During validation Trial 2, a similar mean difference was observed (-0.001±0.006°C), but this appeared to be statistically significant ($p=0.039$) (Figure 1C). Additionally, the LOA of Trial 2 were ±0.012°C. An ICC of 1.00 was found between myTemp and water bath temperature for validation Trial 1 and 2 (both p-values <0.001, Figure 1B & 1D). The SEM between myTemp and water bath temperature was 0.004°C for both trials.

A repeated-measurements ANOVA revealed that the mean difference between the myTemp system and water bath temperature drifted across plateaus ($p<0.001$), with a minor overestimation (0.002°C) at low temperatures (34-38°C) and a minor underestimation (-0.003°C) for higher temperatures (39-44°C) (Table 1).

Test-Retest Reliability. The mean difference between trial 1 and trial 2 was (0.004±0.008°C, LOA= ±0.015°C, Figure 2A), which appeared to be a significant bias ($p<0.001$). Nevertheless, we found a good agreement between both trials based on an ICC of 1.00 for both the comparison between myTemp temperature Trial 1 and 2, and the comparison between the mean myTemp and water bath temperature for Trial 1 and 2 (both p-values <0.001, Figure 2B). A SEM of 0.005°C was found between myTemp temperature Trial 1 and 2.

DISCUSSION

This study examined the validity and reliability of the myTemp ingestible capsule as a method to assess temperature. We found that the myTemp system is a valid technique to measure (water) temperature under controlled circumstances, evidenced by low LOA (± 0.011) and a small mean difference (-0.001±0.005°C) between water bath and myTemp temperature. Furthermore, an excellent test-retest reliability (LOA= ±0.015°C, ICC=1.00 and SEM=0.005°C) was found, in combination with a small, but significant, mean difference (0.004±0.008°C) between Trial 1 and Trial 2. These findings suggest that the myTemp system is useful for (exercise) scientists and clinicians to accurately measure temperature in a non-invasive way.

Criteria have been formulated to determine the validity of novel measurement techniques. Preferably, the accuracy of the measurements is characterized by a I) low systemic bias, II) narrow 95% LOA, III) high ICC with the reference temperature, and IV) low SEM[16]. For assessment of Tc, a thermometer must have an accuracy of approximately 0.1°C without influences of environmental factors[17], in combination with an acceptable level of agreement, described as a systemic bias <0.1°C and 95% LOA within ±0.4°C[9]. Based on the low systemic bias (-0.001°C) and narrow LOA (±0.011°C) we can conclude that the myTemp capsule system is a valid method to assess (water) temperature under controlled circumstances. Although we found a significant systemic bias of -0.001°C between the myTemp and water bath temperature in Trial 2, the difference between both measurements complies easily with the acceptable level of agreement and is clinically and physiologically negligible. Moreover, a change in Tc of ±0.1°C has been established as physiologically and clinically relevant[17]. Furthermore, the mean difference between the myTemp and water bath temperature drifted across the physiological range (34-44°C), with a negligible overestimation (0.002°C) at low temperatures (34-38°C) and a negligible underestimation (-0.003°C) for higher temperatures (39-44°C) However, the drifted response throughout the physiological range complies with the criteria for an acceptable level of agreement, in which a maximal difference of 0.010°C was found between target temperature 34 and 44°C (Table 1). As previous studies have demonstrated that the gastrointestinal temperature is a valid and reliable

surrogate measure for Tc[9, 11, 18], these results suggests that the myTemp temperature capsule is a valid method to assess Tc in different circumstances.

A reliability of 0.004°C was found, accompanied by a narrow LOA (±0.015°C), high ICC (1.00), and low SEM (0.005°C). These findings suggest that the myTemp temperature capsule has a very good test-retest reliability. Typically, an ICC of 0.70 is considered as acceptable, with higher values representing a better reliability[19]. An ICC of 1.00, such as found in current study, suggest that the error variance between both measurements is negligible compared to the normal variance[20]. The significant systematic bias between Trial 1 and 2 is physiologically negligible and is well below the acceptable accuracy level of 0.1°C. Therefore, the myTemp temperature sensor is reliable method to perform repeated core body temperature measurements.

This is the first ex-vivo validation study that compares a telemetric temperature capsule system with the average of four highly sensitive temperature probes across the whole physiological Tc range (34-44°C). In previous validation studies, water bath temperature measured by temperature capsule systems was compared with the water bath temperature measured with less accurate thermometers such as a rectal probe[16] or a mercury thermometer[10]. They found a systemic bias of 0.17±0.15°C (LOA = 0.30°C), 0.23±0.17°C (LOA = 0.34°C), and 0.27±0.09°C for the VitalSense[16], e-Celsius[16] and CorTemp[10] temperature capsule system respectively, which are markedly higher than the bias found for the myTemp system. The higher systemic bias found in these studies can be explained by a less accurate temperature capsule system as well as by the normal variance of a rectal probe or mercury thermometer. Moreover, other instruments to measure Tc (i.e. esophageal or rectal probe, tympanic thermistor) did neither have an accuracy lower than 0.1°C[21]. Therefore, the myTemp temperature capsule may become the preferred method to accurately assess Tc.

The strength of current study is the controlled study protocol, with four highly sensitive wired temperature probes (up to 0.002°C), a stepwise increase in water bath temperature, and the criteria for reaching a stable plateau phase. As in our study, the resolution of the myTemp system was 0.01°C, which is physiologically sufficient for in-vivo measurements in sport and exercise sciences. However, we have to take a limitation into account. Within this study, we only examine the validity and reliability

of the myTemp system in controlled ex-vivo conditions. Therefore, it will be important to examine whether the myTemp system demonstrates a similar accuracy and reliability in less controlled in-vivo circumstances. Furthermore, the study design of our study should be repeated for the other temperature capsule systems, in order to point out the most accurate system to measure the intestinal temperature.

CONCLUSION

Based on the low systemic bias, narrow 95% LOA, high ICC with the reference temperature, and low SEM, we believe that the myTemp ingestible temperature capsule is a valid and reliable technique to measure (water) temperature under controlled circumstances. Moreover, the consistent low systemic bias and low limits of agreement suggest that the myTemp capsule should not be calibrated prior to usage. Future studies investigating the myTemp system in an ex-vivo as well as in-vivo setting in lab- and field conditions are needed to confirm the superiority of this novel temperature system compared to other commercially available products.

PRACTICAL IMPLICATIONS

- An excellent agreement between temperature measured with the myTemp capsule and the water bath temperature was found.
- The myTemp temperature capsule showed a very good test-retest reliability.
- The myTemp system is useful for (exercise) scientists and clinicians to accurately measure temperature in a non-invasive way.

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REFERENCE LIST

1. Mackowiak PA, Wasserman SS, Levine MM. A critical appraisal of 98.6 degrees F, the upper limit of the normal body temperature, and other legacies of Carl Reinhold August Wunderlich. *JAMA.* 1992; 268(12):1578-1580.
2. Wunderlich K. The course of temperature in disease: a guide to clinical thermometry. *The American Journal of The Medical Sciences* 1869; 57:425-447.
3. Tansey EA, Johnson CD. Recent advances in thermoregulation. *Adv Physiol Educ.* 2015; 39(3):139-148.
4. Edwards RHT, Hill DK, Jones DA. Heat Production and Chemical Changes during Isometric Contractions of Human Quadriceps Muscle. *J Physiol-London.* 1975; 251(2):303-315.
5. Gonzalez-Alonso J. Human thermoregulation and the cardiovascular system. *Exp Physiol.* 2012; 97(3):340-346.
6. Gonzalez-Alonso J, Quistorff B, Krustrup P, et al. Heat production in human skeletal muscle at the onset of intense dynamic exercise. *J Physiol-London.* 2000; 524(2):603-615.
7. Glazer JL. Management of heatstroke and heat exhaustion. *Am Fam Physician.* 2005; 71(11):2133-2140.
8. Fulbrook P. Core temperature measurement in adults: a literature review. *J Adv Nurs.* 1993; 18(9):1451-1460.
9. Byrne C, Lim CL. The ingestible telemetric body core temperature sensor: a review of validity and exercise applications. *Br J Sports Med.* 2007; 41(3):126-133.
10. Challis GG, Kolb JC. Agreement Between an Ingestible Telemetric Sensor System and a Mercury Thermometer Before and After Linear Regression Correction. *Clin J Sport Med.* 2010; 20(1):53-57.
11. Gant N, Atkinson G, Williams C. The validity and reliability of intestinal temperature during intermittent running. *Med Sci Sport Exer.* 2006; 38(11):1926-1931.
12. O'Brien C, Hoyt RW, Buller MJ, et al. Telemetry pill measurement of core temperature in humans during active heating and cooling. *Med Sci Sport Exer.* 1998; 30(3):468-472.
13. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet.* 1986; 1(8476):307-310.
14. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. *Psychol Bull.* 1979; 86(2):420-428.
15. Hopkins WG. Measures of reliability in sports medicine and science. *Sports Med.* 2000; 30(1):1-15.
16. Travers GJ, Nichols DS, Farooq A, et al. Validation of an ingestible temperature data logging and telemetry system during exercise in the heat. *Temperature (Austin).* 2016; 3(2):208-219.
17. Moran DS, Mendal L. Core temperature measurement: methods and current insights. *Sports Med.* 2002; 32(14):879-885.
18. Lim CL, Byrne C, Lee JK. Human thermoregulation and measurement of body temperature in exercise and clinical settings. *Ann Acad Med Singapore.* 2008; 37(4):347-353.
19. Nunnally JCB, I.H. *Psychometric Theory,* 3rd ed, New York, McGraw-Hill; 1994.
20. de Vet HCWT, C.B.; Mokkink, L.B.; Knol, D.L. *Measurement in Medicine,* 3rd ed, New York, Cambridge University Press; 2014.
21. Robinson J, Charlton J, Seal R, et al. Oesophageal, rectal, axillary, tympanic and pulmonary artery temperatures during cardiac surgery. *Can J Anaesth.* 1998; 45(4):317-323.

FIGURE LEGENDS

Figure 1. Bland-Altman plot of myTemp *versus* water bath temperature for Trial 1 **(A)** and Trial 2 **(C)**. Data were presented as mean difference (solid red line) ± LOA (dotted red line). Furthermore, a bi-variate correlation was plotted for both Trial 1 **(B)** and 2 **(D)**, in which the myTemp temperature (x-axis) was plotted versus the water bath temperature (y-axis). The negligible systematic bias in both trials suggests a good agreement between myTemp and water bath temperature, while the ICC of 1.00 suggests an excelling accuracy of the myTemp system.

Figure 2. Bland-Altman plot of Trial 1 *versus* Trial 2 **(A)**. Data were presented as mean difference (solid red line) ± LOA (dotted red line). A significant, but physiological and clinical negligible, systematic bias was found between myTemp and water bath temperature. Furthermore, the bi-variate correlation plot **(B)** of Trial 1 (x-axis) and Trial 2 (y-axis) suggests an excellent agreement between Trial 1 and Trial 2.

SUPPLEMENTARY FIGURES

Supplementary Figure 1. Schematic overview of study protocol with temperature plateaus

Supplementary Figure 2. Overview of the study set-up

Figure 1.

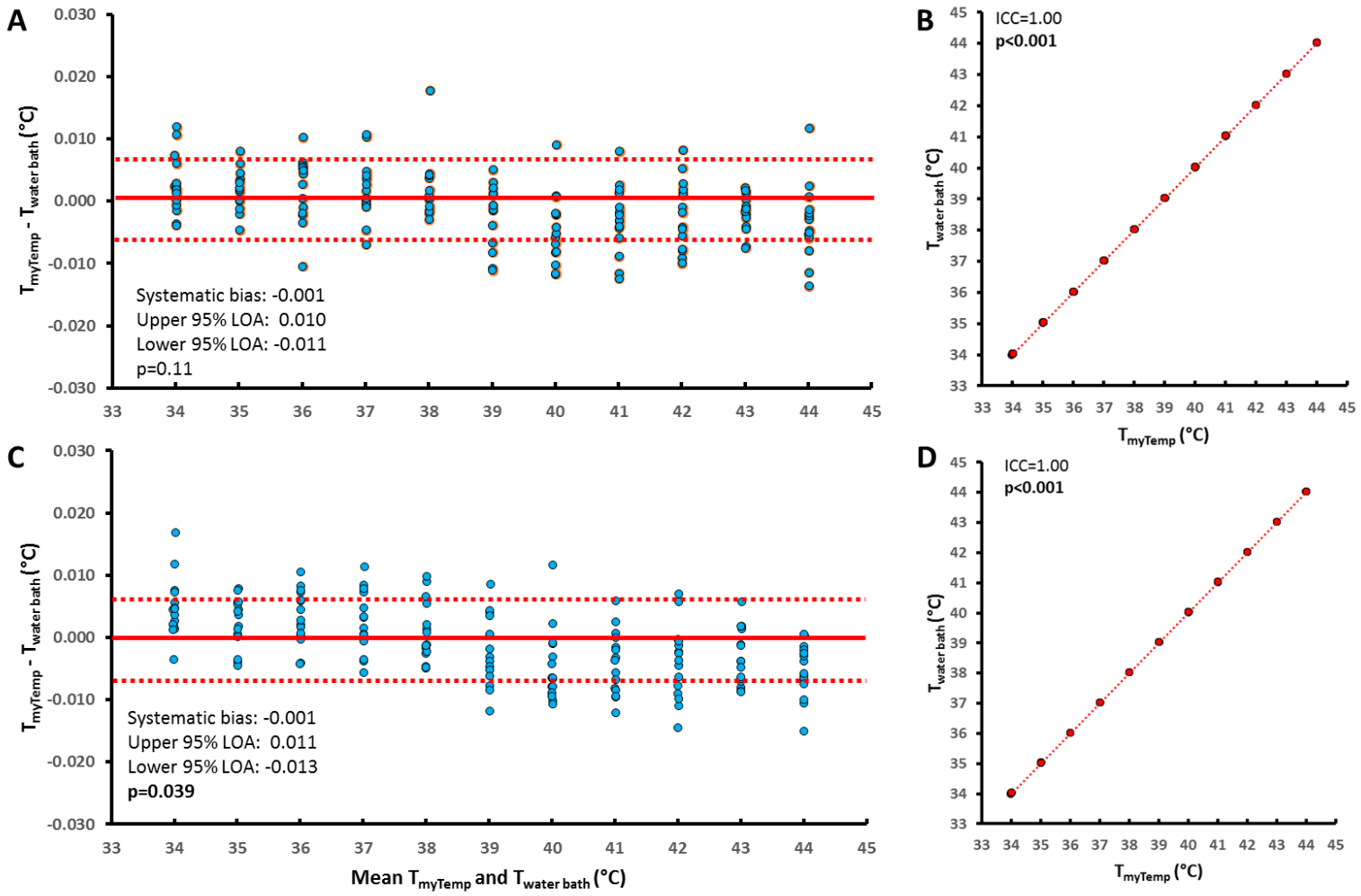
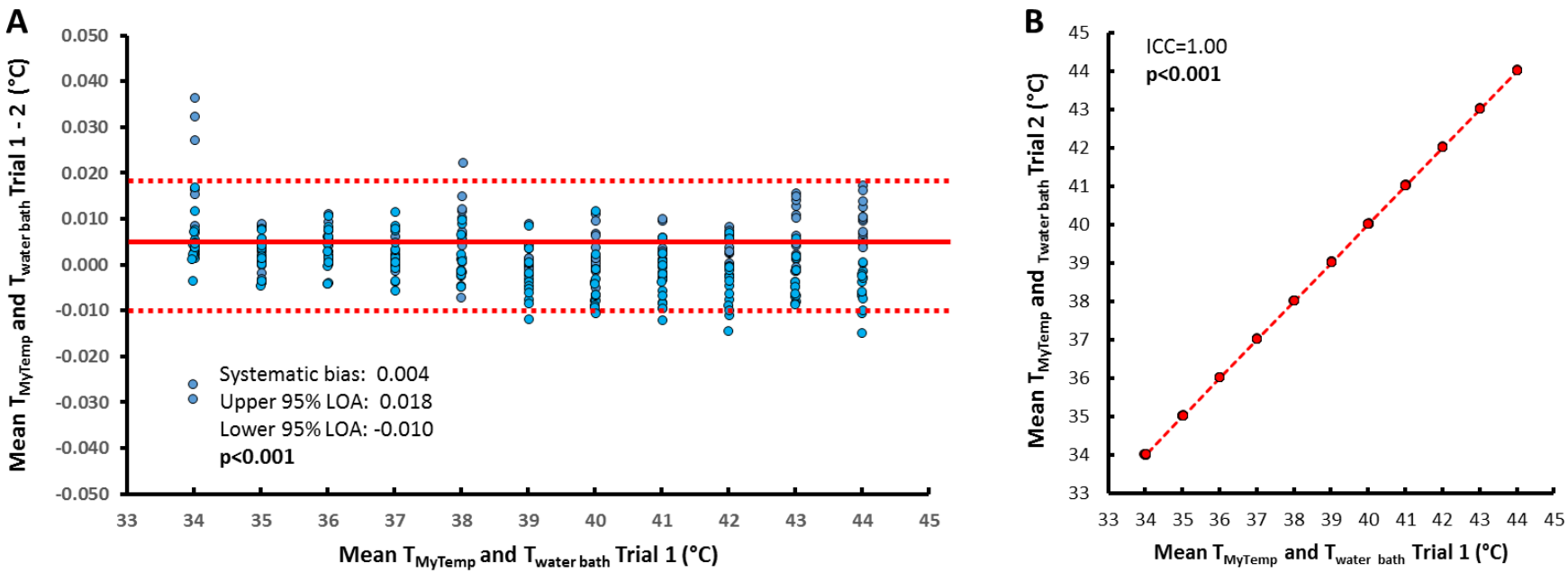

A
0.030
0.020
0.010
0.000
-0.010
-0.020
-0.030
T_{myTemp} - $T_{water\ bath}$ (°C)
Systematic bias: -0.001
Upper 95% LOA: 0.010
Lower 95% LOA: -0.011
p=0.11
33 34 35 36 37 38 39 40 41 42 43 44 45
B
ICC=1.00
p<0.001
$T_{water\ bath}$ (°C)
T_{myTemp} (°C)
C
Systematic bias: -0.001
Upper 95% LOA: 0.011
Lower 95% LOA: -0.013
p=0.039
Mean T_{myTemp} and $T_{water\ bath}$ (°C)
D
ICC=1.00
p<0.001

Figure 2.


A
Mean T_{MyTemp} and $T_{water\ bath}$ Trial 1 - 2 (°C)
0.050
0.040
0.030
0.020
0.010
0.000
-0.010
-0.020
-0.030
-0.040
-0.050
Systematic bias: 0.004
Upper 95% LOA: 0.018
Lower 95% LOA: -0.010
p<0.001
33 34 35 36 37 38 39 40 41 42 43 44 45
Mean T_{MyTemp} and $T_{water\ bath}$ Trial 1 (°C)
B
Mean T_{MyTemp} and $T_{water\ bath}$ Trial 2 (°C)
ICC=1.00
p<0.001
45 44 43 42 41 40 39 38 37 36 35 34 33
33 34 35 36 37 38 39 40 41 42 43 44 45
Mean T_{MyTemp} and $T_{water\ bath}$ Trial 1 (°C)

Supplementary Figure 1.

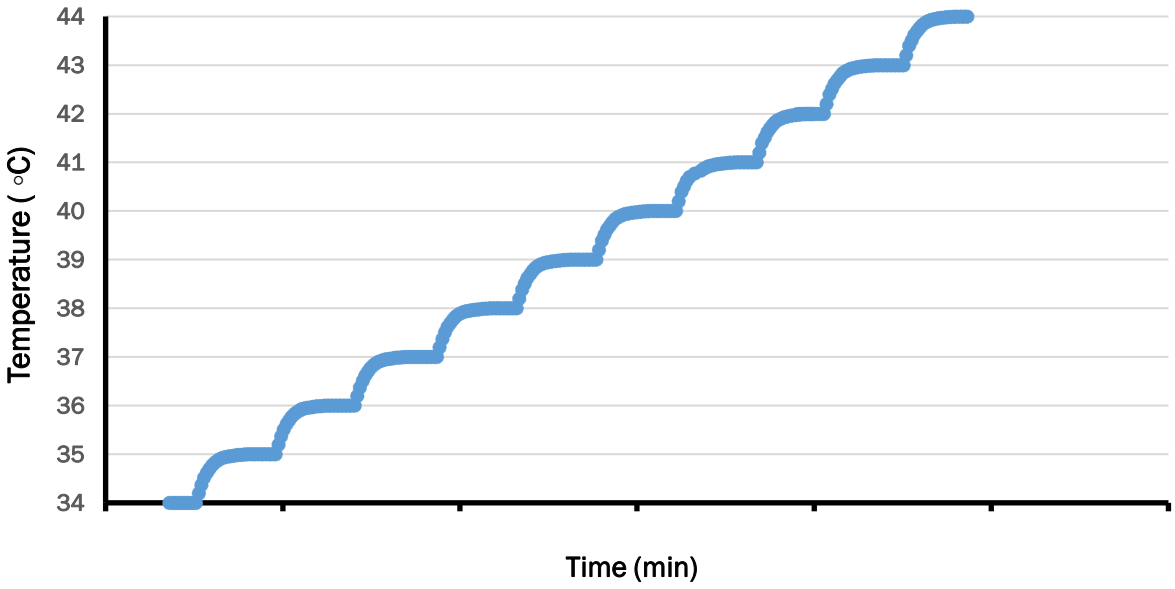


Table 1. Difference between water bath and myTemp temperature (Δ Water bath –myTemp) throughout the temperature range. Data are presented as averages from n=15 capsules that were measured during two separate trials.

	Trial 1		Trial 2	
Target Temperature	**Δ Water bath - myTemp (°C)**	**p-value***	**Δ Water bath - myTemp (°C)**	**p-value***
34	0.003 ± 0.005	0.06	0.005 ± 0.005	**0.002**
35	0.002 ± 0.003	0.06	0.002 ± 0.004	**0.042**
36	0.002 ± 0.005	0.15	0.003 ± 0.004	**0.013**
37	0.002 ± 0.005	0.20	0.002 ± 0.005	0.10
38	0.002 ± 0.005	0.17	0.001 ± 0.005	0.58
39	-0.002 ± 0.005	0.12	-0.002 ± 0.006	0.16
40	-0.005 ± 0.006	**0.006**	-0.005 ± 0.006	**0.008**
41	-0.003 ± 0.005	**0.048**	-0.004 ± 0.005	**0.007**
42	-0.002 ± 0.005	0.15	-0.004 ± 0.006	**0.017**
43	-0.002 ± 0.003	**0.038**	-0.003 ± 0.004	**0.012**
44	-0.003 ± 0.006	**0.042**	-0.005 ± 0.004	**<0.001**

Repeated measures ANOVA revealed a significant difference in Δ water bath – myTemp temperature across the temperature range ($p<0.001$ for both Trial 1 and Trial 2). * Represents the p-value for the post-hoc one sample t-test analysis.