The non-invasive TEMPLE TOUCH PRO™ system is an accurate and reliable device compared to continuous invasive reference methods during surgery

Rambam hospital, Wolfson hospital and Schneider hospital in Israel

Background

Today's current technology for continuously measure core body temperature is by using nasopharyngeal, esophageal or rectal temperature probe. These probes are invasive and must be placed by a professional, typically an anesthesiologist. Intraoperative core temperature monitoring is standard-of-care because prompt diagnosis and management of thermal disturbances may prevent complications.

Present-day standards of care for determining patient core body temperature are inhibited by a compromise between invasiveness and accuracy. Core body temperature is defined as "the temperature of the blood bathing the hypothalamus". Performing this measurement on a live patient is not feasible, so current means for accurate measurements require contact with the body's other highly perfused core organs. These methods include esophageal, nasopharynx, and pulmonary artery thermometers. Though highly accurate, these measurements are only practical when the patient is placed under general anesthesia and can result in irritation at the applied site on waking. For localized anesthesia, the best options for temperature monitoring are at so-called "near-core" locations. These sites include skin-surface, rectal, axillary, oral, and tympanic methods. However, these locations are located further from the defined core temperature, so factors such as environmental temperature affect the measured temperature. Thus, such measurements are not as accurate nor are able to detect temperature fluctuations as rapidly as the more invasive methods.

Identifying the need for non-invasive core body thermometry, companies such as 3M (SpotOn) have been offering zero-heat-flux thermometers. These thermometers claim an accuracy of 0.5°C (the consensus for clinically acceptable accuracy but need approximately 10 minutes to achieve equilibrium, meaning they are not useful for extreme temperature fluctuations that can occur during cardiac surgery, for example. Additionally, zero-heat-flux thermometers do not work at temperatures less than 32°C, which is well within the temperature range for life, namely 18°C to 46°C. [1]

Ref [1]: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943173/

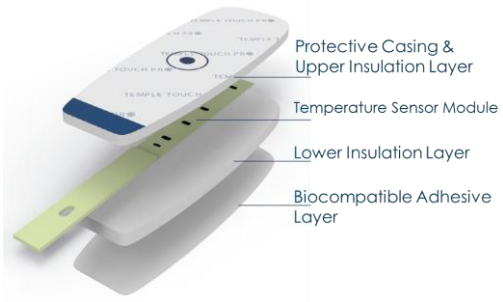
Temple Touch Pro (TTP)

The Temple Touch Pro (TTP) developed and manufactured by Medisim Ltd is a relatively new system that estimates core body temperature from the temple, using heat flux rather than zero-heat-flux. The TTP system allows a non-invasive, continuous monitoring of the core body temperature. The core body temperature is calculated by special mathematical algorithm, based on the conductive heat flux technology for determination of core body temperature.

Figure 1: Measurement Method

Heat Flux Technology

Temple Touch Pro (TTP) sensor unit measures heat flux from blood to the skin, and using a proprietary algorithm, core temperature is derived.



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Objective

The purpose of this clinical study was to demonstrate that there is no statistically significant difference between temperatures measured by TTP and by invasive thermometers. Furthermore, a secondary aim was to demonstrate the effectiveness and safety of the TTP for measurements on patients' temple area of the forehead. In order to achieve these goals, the trial was conducted among various populations (different age groups, genders and operations) and compared to various reference measurements.

The study endpoints were:

- Efficacy indicated by correlation to reference gold standard – TTP temperature reading will be in good correlation with the reference device be >0.9.

- Safety – no serious adverse effects will result from use of TTP.

Method

This clinical trial was performed in compliance with ISO 80610-2-56 and GCP standards. The study was performed at Rambam hospital, Wolfson hospital and Schneider hospital in Israel, with the approval of the Helsinki Committee (section 3). The clinical trials were conducted with TTP system (SU & MCU- the MCU has logger for recording data) and in accordance with the clinical trial protocol (section 3). For the clinical trial the MCU had also an optional input connection used for the reference sensor. Thus, both body temperatures (the TTP system output and the reference) were recorded during the measurements simultaneously.

An informed consent was obtained from each patient prior to surgery. In the operating room, each patient's temperature was measured with both the TTP and another continuous reference methods used clinically for measuring the core temperature: esophageal (Novamed, New York, NY, USA), rectal (Measurement Specialties Inc., Galway, Ireland) or nasopharyngeal (DS Medical, Hampshire, UK) temperature sensor. In case that the patient was not under anesthesia, the reference measurement was taken using intermittent thermometer– Sure Tempe Plus® by Welch Allyn® measuring in Oral, Axillar or Rectal modes.

The TTP Sensor Unit was attached to the patient's temple area of the forehead by professional staff trained by Medisim, immediately after the anesthetization of the patient. Concurrently, reference temperature probes were inserted by the anesthesiologist. The TTP Sensor Unit sampled the patient's temperatures and data was recorded by the TTP System, which was also connected to a vital sign monitor that displayed the patient's temperature. Patient's temperature was monitored during the entire surgery. After the surgery the data was downloaded for further analysis.

Before the initiation of the clinical trial, the TTP™ accuracy was verified in a calibrated water bath that meets the specifications of the ASTM E 1112-00 and EN 12470-4 standards.

Confirmation of the safety of use was indicated by instructing the study staff, subjects, parents or study monitors to report on any safety issue.

Table 1: Study Population (n=152)

Age	Patients 0-73 years old (median age was 4).
Gender	84 males and 68 females.
Undergoing	Major surgeries such as cardiothoracic, abdominal, orthopedic, gynecological, oncology and general surgeries.

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Result

Following is the statistical analysis of the clinical trial results. The statistical analysis was performed using the AnalyzeIt software (v2.30 Excel 2003).

The first part of the analysis consisted in calculating the main values: average difference between TTP and Reference, average absolute difference between TTP and Reference, correlation between TTP™ & Reference and Pooled standard deviation. These results present in Table 2.

We used Bland-Altman method for agreement analysis and linear regression analysis. The results of these analyses are in Table 3 and Figures 2-3.

Correlation analysis (Table 2) yielded a Pearson correlation coefficient of 0.91, and pooled standard deviation of 0.07 °C, in order to prove the clinical repeatability of the TTP™ system.

Table 2*:* Difference and Correlation Between TTP™ and Reference

	Values
Average difference from reference [°C]	0.035±0.29
Average absolute difference from reference [°C]	0.23±0.18
Pooled STD [°C]	0.07
Pearson correlation between TTP & Reference	0.91

Table 3*:* Bland Altmann Summary Data

	TTP™ system Vs. Reference	
n (# of measurements)	4307	
Correlation - absolute difference v average	0.1054	
Bias	0.035	
95% CI	0.026 to 0.0436	
SE	0.0044	
t statistic	7.93	
DF	4306	
p	<0.0001	
SD of differences	0.289 between single measurements	
	95% Limits of agreement	***95% CI***
Lower	-0.532	-0.547 to -0.517
Upper	0.602	0.587 to 0.617

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Figure 2*:* Scatter plot of temperature measurements using TTP system versus core temperature, including the line of equality (N = 152).

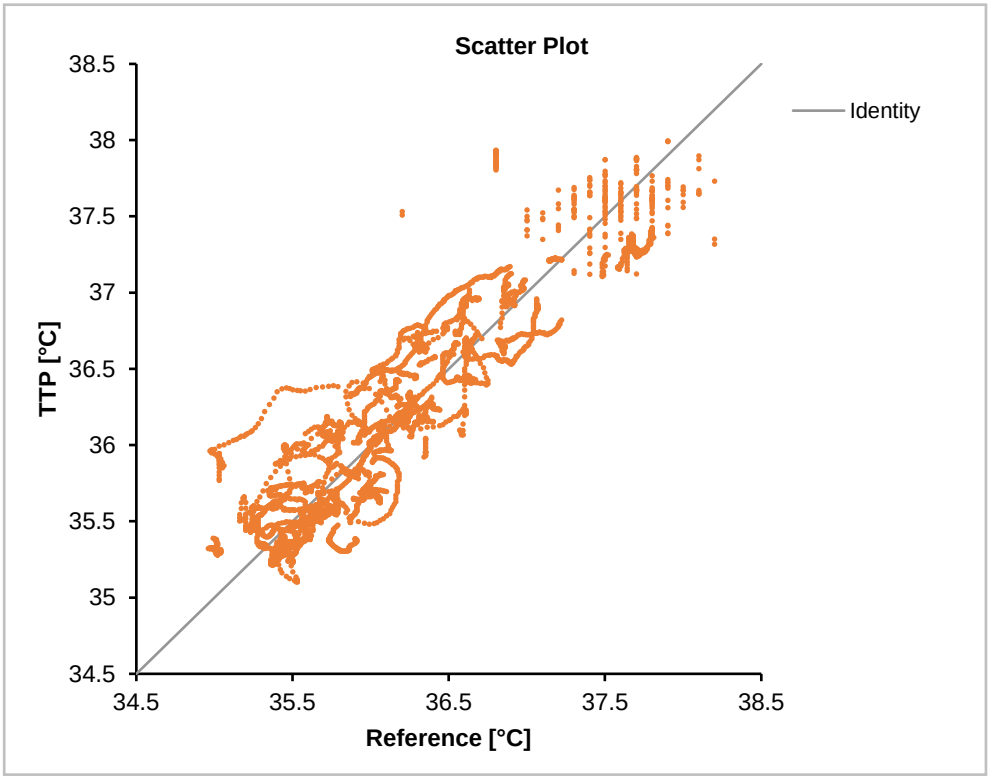
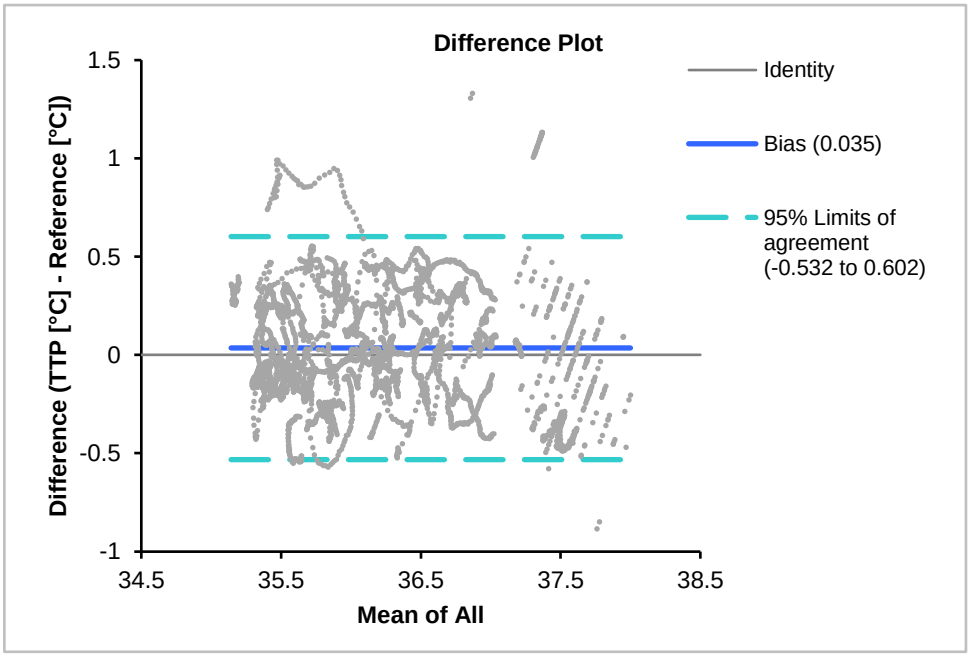


Figure 3*:* Bland-Altman plot of TTP system versus core temperature. Limits of agreement (dashed lines) on the plot infer where 95% of differences between the two methods are expected to fall.



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Discussion

The TTP system demonstrates a very good accuracy: the average difference from reference measurements are 0.035±0.29ºC. It should be noted that the optimal clinical accuracy, for continues temperature monitoring in the literature is determined as 0.5°C.

The scatter plot of the TTP measurements versus core temperature (Figure 2) suggests a strong positive linear correlation between the two methods, which (importantly) is centered on the 45-degree line of agreement. The Bland Altman plot (Figure 3) shows that the limits of agreement are reasonably narrow. There was no strong evidence increasing or decreasing systematic bias (i.e., mean difference) or variability (i.e., spread) between the TTP and the reference measurements as temperature increases. The estimated limits of agreement were (-0.532ºC, 0.602ºC), indicating good TTP-reference agreement across an observe range of mean temperature (i.e., average of TTP and reference) from 35.14ºC to 38ºC.

Pearson correlation test reveals high correlation (0.91) between TTP and the reference, which indicates good performance of the TTP. The Pooled standard deviation which is the geometrical average of the standard deviation calculated for each patient, supports this conclusion; pooled standard deviation of 0.07ºC means that the deviation between repeated measurements is very low, that confirms the TTP system is repeatable.

From the clinical report of TTP, all 152 patients that were exposed to the TTP system were found safe to both user and subject. The device was used safely without causing any discomfort to the patients. There were no observations or reports of any adverse events during the evaluation trials. None of the patients left the trial. No allergy symptoms, skin irritation or discomfort of patients was reported.

Conclusions

The results of this study show the following:

1) The non-invasive TTP system is an accurate and reliable device compared to continuous invasive reference methods during surgery.

2) Use of the TTP system is safe and without any discomfort to the patients. There were no observations or reports of adverse effects.

3) The TTP materials that are in contact with the human tissues or body fluids are known as biocompatible.

4) These results validate the clinical use of the TTP system on the temple-forehead as a measurement site.

5) TTP system is easy to use, relieves the anesthesiologist and prevents injury and contamination (due to the non-invasive and disposable patch).

Disclosures

Statistical evaluation of clinical trial results was performed by Moshe Yarden, Medisim's CTO.