Research Square

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Continuous temperature monitoring using a non-invasive sensor in patients with febrile neutropenia: a feasibility study

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Abstract

Objective

To develop and test a non-invasive, low-cost continuous temperature monitoring device for use in hospitalized neutropenic oncology patients.

Methods

This research is an analytical, observational, prospective, short-term follow-up, proof-of-concept study conducted in a university hospital. The device, consisting of a thermistor connected to a microcontroller, records temperatures every 10 minutes and transmits the data via Wi-Fi to a database accessible in real time. Initial tests were performed on healthy volunteers and subsequently on adult neutropenic patients hospitalized in a university hospital. The temperature obtained by the device was compared to conventional monitoring performed by the healthcare team. Fever was defined as an axillary temperature ≥ 37.8ºC for both methods.

Results

Thirty-nine neutropenic patients were included, with a mean age of 47 years (SD ± 18), of whom 18 (46.2%) were male and 21 (53.8%) were female. The mean monitoring time was 62 hours (SD ± 22h). Among the seven patients who developed sepsis or septic shock, the device identified fever more quickly in five of them, with a median of two hours (Q1-Q3 = 30 min – 4h37 min) before conventional monitoring. Cluster analysis showed that patients with higher temperature curves, regardless of whether they had reached the fever threshold, showed a higher infection rate and length of hospital stay.

Conclusion

The continuous monitoring device was effective in the early detection of fever in neutropenic patients. Its use can optimize therapeutic measures, potentially reduce complications and improve clinical outcomes in high-risk patients.

1. Introduction

Fever is often the first, and in some cases the only sign of infection in oncohematological patients undergoing high-dose chemotherapy, and it is considered a medical emergency when neutropenia is present [1, 2]. Hospital mortality associated with infection in neutropenic patients ranges from 50% to 75%, highlighting the severity of this condition and the need for effective strategies for its early detection [3].

Febrile neutropenia is commonly associated with bacterial infections and can progress to sepsis or septic shock, both with high mortality in this population [1, 4]. Given the severity of this clinical condition,

an immediate approach is recommended, including blood culture collection and early institution of broad-spectrum antibiotic therapy, aiming to minimize the risk of adverse outcomes [5].

Despite the relevance of rigorous thermal monitoring, its implementation in hospital practice faces considerable challenges. The frequency of temperature measurements depends directly on the patient's severity and the availability of the care team in the ward setting, which can result in delays or failures in identifying febrile episodes [6, 7].

In this context, technologies that enable a continuous, automated, and non-invasive monitoring of body temperature emerge as promising alternatives for the early detection of fever and the optimization of clinical outcomes. These technologies are capable of reducing delays in fever identification and, consequently, of speeding up the administration of antibiotic treatment, with the potential to reduce the need for hospitalization and transfers to intensive care units (ICUs) [8–11].

The present study aimed to develop and test a non-invasive and low-cost continuous body temperature monitoring device for use in neutropenic oncology patients hospitalized in a university hospital infirmary.

2. Methodology

This was an analytical, observational, prospective, short-term follow-up, proof-of-concept study, conducted in a university hospital in Belo Horizonte, Brazil, and developed in three stages. In the first stage, the structure, system requirements, and equipment necessary for remote temperature monitoring of patients hospitalized in an infirmary were defined. As a basis for the project, a conceptual model of a multiplatform structure was conceived, allowing for the future integration of new technologies. This model was structured in modules corresponding to three processing environments: i) the location for capturing vital signs, ii) the interface for observation and monitoring by healthcare professionals, and iii) the back-end structure for data storage and processing.

2.1. Development of the monitoring device and structuring of the data communication network.

The developed monitoring device consists of a thermistor, responsible for capturing body temperature, connected to an ESP32 microcontroller, which performs data acquisition and interpretation. The collected information is transmitted via Wi-Fi connection from a local network to a database hosted on a Raspberry Pi. Subsequently, the Raspberry Pi retransmits the data, also via Wi-Fi, to an interface accessible by computer, smartphone, or tablet, ensuring that the care team can view the information in real time using login and password (Fig. 1).

The thermistor is attached to the individual's armpit, secured with hypoallergenic tape, and connected to the device containing the microcontroller, which in turn converts the reading of the collected data into temperature.

The equipment was programmed to measure the patient's temperature every 10 minutes, recording and storing the information, which is sent to a database via a restricted and protected local network for access by the research team, using individual logins and passwords. The data was made available on a supervisory screen (computer, tablet, or cell phone). After access, the user could monitor the temperature measurements of active patients in real time, as well as the measurement history (Fig. 2).

2.2. Testing on healthy volunteers

In this stage, the device was tested on two adult volunteers of different sexes, with no signs of acute illness, to evaluate its technical feasibility and ergonomics. To verify the reliability and reproducibility of the collected and transmitted data, the volunteers simultaneously used a standardized conventional digital thermometer (G-Tech, G-Tech Center Medical, São Paulo, Brazil), enabling a comparison between the recorded temperatures. In this phase, measurements were programmed to occur every minute. During the test, the device was carried by the volunteers in a pouch, which hosted the microcontroller case, ensuring the stability of the equipment during data collection (Fig. 3).

2.3. Testing in hospitalized neutropenic patients

The trial in neutropenic patients was conducted in two inpatient units of the Hospital das Clínicas of the Universidade Federal de Minas Gerais (HC-UFMG), in Belo Horizonte, Brazil, where the monitoring network was structured. Patients included in the study wore the device stored in a pouch for a minimum of 48 hours. In addition, they received a standardized conventional digital thermometer (G-Tech, G-Tech Center Medical, São Paulo, Brazil) for systematic bedside temperature measurement, performed by the care team according to medical prescription. Standardization of the thermometer sought to minimize temperature variations resulting from the use of thermometers from different brands, a common practice at the institution.

The remote monitoring equipment was calibrated at the time the patient was linked to the system, using the digital thermometer as a reference. Calibration was performed through three sequential temperature measurements, at a one-minute interval, enabling comparison between the values recorded by the digital thermometer and the system under test. From this point, measurements were programmed to occur every 10 minutes.

Patients who met the following criteria were included in the study: i) age ≥ 18 years; ii) diagnosis of neutropenia (neutrophils < 500 cells/mm³ or between 500 and 1000 cells/mm³ with a prospect of decreasing to < 500 cells/mm³ within the next 48 hours) on the day of inclusion in the study; iii) diagnosis of active oncological, solid organ, or hematological disease; iv) agreement to participate in the study by signing the Informed Consent Form.

Patients who presented one or more of the following criteria, recorded in a questionnaire administered during data collection, were excluded from the study: i) critical clinical condition or presence of signs of worsening at the time of invitation to participate in the study; ii) poor adherence to monitoring, such as

recurrent disconnection of the thermistor cable from the case to avoid using the device; iii) monitoring for less than 48 hours; iv) equipment failure for a period that made monitoring evaluation impossible for at least 48 hours; and vi) occurrence of an adverse event during monitoring, such as an allergic reaction to the fixation material.

Patients potentially eligible for the study were evaluated weekly to verify if they met the inclusion criteria. To this end, the research team conducted daily active searches in the electronic medical records of patients hospitalized in two inpatient wards (total 57 beds) where the monitoring network was structured to confirm the diagnosis of neoplasia, as well as the analysis of laboratory tests to identify neutropenia. Once a patient meeting the laboratory criteria for inclusion was identified, the research team would visit the wards of the inpatient units to assess eligibility and, if confirmed, invite the patient to participate in the study.

Eligible patients who agreed to participate in the research and signed the Informed Consent Form were included and their monitoring began. The frequency of patient temperature measurement by the nursing staff followed the prescription of the attending physician, generally performed every six hours. In some cases, specific prescriptions required a more rigorous temperature curve, with temperature measurement every four hours.

According to the care protocol used at HC-UFMG, fever in neutropenic patients is an axillary temperature ≥ 37.8°C. The choice to consider a value below 38°C, adopted in the international literature (IDSA guideline), is due to the intention of maintaining the sensitivity of this clinical sign, given that in Brazil axillary temperature is routinely used, whose values are lower than those of oral temperature [12]. The occurrence of fever through monitoring performed by the nursing staff was defined in consultations made in the electronic medical records of the patients included in the study. Patients were monitored daily by the research team while wearing the monitoring device. Data for a period of 14 days from the installation of the equipment were obtained through the analysis of electronic medical records to extract information regarding the following outcomes: identification of fever as a consequence of an infectious condition, need for transfer to an ICU, hospital discharge, and death. In addition, for patients who survived the infection analyzed in the clinical outcome, follow-up was conducted throughout their hospitalization to determine the length of hospital stay.

2.4. Statistical analysis

The collected data were recorded on the Redcap – Research Electronic Data Capture platform (Vanderbilt University, USA). Analyses were performed using IBM SPSS Statistics 20 [13] to verify the association between patient outcomes and temperature curves. Categorical variables were expressed as percentages, and continuous variables were presented using mean (standard deviation) or median (Q1 – Q3), according to the distribution (normal or non-normal). Qualitative variables were compared using Chi-square tests or Fisher's exact test, and continuous variables using Student's t-test or Mann-Whitney U test, as indicated. The McNemar test was used to compare the proportion of fever detection by nursing staff and by the device. The significance level adopted in all analyses was 5%, two-tailed.

Furthermore, for the analysis of thermal patterns over time, a cluster analysis was performed using the Network Node Dispersion method. Initially, 15,444 temperature measurements were collected and underwent a filtering process to ensure data quality. Measurements considered invalid were excluded, i.e., those with values below 35.0°C or above 42.0°C. After this data filtering, the remaining measurements were subjected to cluster analysis, resulting in the separation into two distinct groups with approximately the same temperature within each cluster. This procedure enabled the identification of similar patterns in temperature evolution during the time series, allowing for a more detailed understanding of patients' thermal variations and their possible association with clinical outcomes.

To complement the analyses, graphs were generated using R software, version 4.4.1, to compare the fever detection time by the nursing staff and by the monitoring device.

2.5. Ethical aspects

The study was approved by the UFMG Ethics and Research Committee (*Comitê de Ética e Pesquisa* – COEP) (CAAE: 54215716.8.0000.5149) and Informed Consent Forms were offered to the research participants who were included in the study.

3. Results

Details regarding the preliminary development stage and initial testing of the device on healthy volunteers are presented as Supplementary Material.

3.1. Testing in neutropenic patients

The system was first evaluated in six hospitalized neutropenic adult patients, which allowed for adjustments to be made in the uncontrolled infirmary setting, including data storage and reliability, system usability, signal transmission stability in the closed network of the selected infirmaries, and the adequacy of sensor fixation on the patients. These patients were not included in the final analysis of the study.

Over the course of 24 months of study, 99 patients were invited to participate in the study, of whom 49 accepted and were included (Fig. 4). Of these, 10 (20.4%) patients were excluded: 4 patients (8.1%) dropped out of the monitoring process before completing 48 hours with the equipment; 2 patients (4%) were excluded due to equipment failures related to signal transmission; and 4 patients (8.1%) showed low adherence to the use of the device during monitoring (Fig. 4).

Of the 39 patients included in the final analysis of the study, 18 (46.2%) were male and 21 (53.8%) were female, with a mean age of 47 years (SD ± 18). The most frequent diagnosis was acute myeloid leukemia, present in 20 patients (51.3%), followed by acute lymphoblastic leukemia, with 9 cases (23.1%). Other diagnoses included lymphoma, multiple myeloma, myelodysplastic syndrome, and solid organ neoplasm. The most prevalent mechanism of neutropenia was post-chemotherapy, observed in 25

patients (64.1%), of whom 12 (30.8%) presented severe neutropenia (< 100 neutrophils). The main characteristics of the patients included in the study are shown in Table 1.

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Table 1
Clinical characterization of the population included in the study.

Variable	N	%
Gender		
Male	18	46.2
Female	21	53.8
Age range		
20–29	8	20.5
30–39	7	17.9
40–49	5	12.8
50–59	5	12.8
> 60	14	35.9
Diagnosis		
Acute Myeloid Leukemia	20	51.3
Acute Lymphoblastic Leukemia	09	23.1
Lymphoma. Multiple Myeloma. Myelodysplasia. Solid Neoplasm	10	25.6
Mechanism of Neutropenia		
Primary	8	20.5
Post-chemotherapy	25	64.1
Secondary to other causes	6	15.4
Intensity of Neutropenia		
Mild (500–1000)	14	35.9
Moderate (100–499)	6	15.4
Severe (< 100)	19	48.7
Infection during 14-day follow-up		
No	21	53.8
Non-serious infection	11	28.2
Sepsis	4	10.2
Septic Shock	3	7.6

Following a 14-day follow-up, it was found that 18 patients (46.2%) presented microbiologically confirmed infection. Of these 18 patients, 11 (61.1%) developed non-severe infection, while 4 (22.2%) progressed to sepsis and 3 (16.7%) to septic shock. Furthermore, in this same subgroup of 18 patients, 6 patients (33.3%) required transfer to an ICU and 2 (5.1%) died.

Regarding the portability and ergonomics of the device, a specific questionnaire was applied to the 39 patients included in this study. The comfort assessment was classified as good by 71.8% (n = 28), very good by 17.9% (n = 7), and excellent by 7.7% (n = 3), while 2.6% (n = 1) did not provide an opinion. Regarding the esthetics of the device, 23.1% (n = 9) of the patients considered it good, 5.1% (n = 2) very good, and 10.3% (n = 4) excellent, while 59% (n = 23) did not express an opinion. Regarding suggestions for improvement, 28.2% (n = 11) indicated that the absence of wires would make the device better, 5.1% (n = 2) suggested improvements in the fixation to avoid limitations in movement, 12.8% (n = 5) pointed out the need to reduce the size, and 2.6% (n = 1) suggested a lighter model. However, 48.7% (n = 19) did not comment on this aspect. Finally, less than half (46.2%) of the participants stated that they would use the device again in its current form.

3.2. Fever and clinical outcomes

In the 39 patients included, a total of 11,291 temperature records were obtained through remote monitoring, resulting in an average of 290 measurements per patient. The average monitoring time was 62 hours (SD ± 22 hours). As expected, the number of temperature measurements ≥ 37.8°C detected by the remote monitoring device was significantly higher than the number detected by the nursing staff (896 [98.03%] vs. 18 [1.97%]; $p < 0.001$). The average number of temperature measurements ≥ 37.8°C during hospitalization in this study population was 22.97 (SD ± 40.30) by the remote device, while routine care recorded 0.46 (SD ± 1.16) fever measurements per patient.

When comparing the febrile episode detection rate, which is the ratio between the number of febrile episodes detected and the total measurements taken, no difference was observed between the two methods; 2.56% by the remote monitoring device; and 2.55% by the nursing staff. Regarding the number of patients who presented fever during the monitoring period, the remote monitoring device identified this sign in 20 patients (51.2%), as compared to 8 (20.5%) by the nursing staff ($p = 0.013$). All febrile events documented by nursing staff were also detected by the device being tested. Among the patients in whom both methods detected fever, four showed signs of worsening, requiring admission to an ICU, and of these, two died. Additionally, two patients in whom only the device identified fever were transferred to an ICU.

3.3. Cluster analysis

Cluster analysis was performed, including all temperature measurements monitored by the device being tested, categorizing patients into two distinct groups (Fig. 5). The comparison between these two groups revealed a statistically significant association between the thermal curve pattern and the occurrence of infection, i.e., patients with higher thermal curves (Fig. 5 – red color) presented a diagnosis of infection more frequently throughout the 14 days of observation, when compared to the cluster with lower

temperatures (Fig. 5 – green color) (14 cases [66.7%] red color vs. 4 cases [25.0%] green color, respectively; p = 0.012). In addition, the first subgroup (red color) presented a significantly longer length of hospital stay in days (47 [33–65] vs. 31.5 [22–41]; p = 0.016).

In this analysis, it was found that seven (33.3%) of the 21 patients in the subgroup with a tendency towards higher temperatures (red color) developed sepsis or septic shock, which did not occur in any of the 18 patients in the other subgroup (green color) (p = 0.009). In four of these seven patients, fever was detected by both the device and the nursing staff, allowing for a comparison of the time difference for fever detection between the two methods. Thus, the median interval for detecting the first fever episode between the device and the nursing records was two hours (Q1-Q3 = 30 min – 4h37 min). As shown in Fig. 6, the time intervals between these measurements per patient were as follows: 8 hours for patient ID1, 30 minutes for patients ID2 and ID15, and 3 hours and 30 minutes for patient ID30.

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4. Discusion

In this feasibility study, a non-invasive device for continuous temperature monitoring in hospitalized neutropenic cancer patients was developed and tested, focusing on the early detection of fever. The use of the remote monitoring device proved feasible and enabled an earlier identification of fever when compared to measurements performed by the nursing staff in routine care. Furthermore, patients with higher temperature curves, even if not reaching fever cutoffs, presented a higher frequency of infectious complications, including sepsis and septic shock, as well as longer hospital stays, a greater need for ICU transfer, and death.

Fever in neutropenic patients can indicate serious infection, and requires immediate recognition and treatment to prevent complications, such as sepsis and septic shock [2]. The continuous monitoring technology tested in this study proved to be a promising strategy by enabling a real-time detection of febrile episodes, reducing reliance on intermittent measurements and potentially anticipating medical interventions [14]. It is important to emphasize that this was an observational study and that no intervention guided by the device being tested were performed; the procedures were dictated by routine care, exclusively defined by the attending medical team.

Among the seven patients who presented sepsis or septic shock, four had fever detected by the device in a median of two hours (Q1-Q3 = 30 min – 4h37 min) before manual recording by the nursing staff. This temporal difference suggests that continuous monitoring can anticipate the identification of this sign and avoid delays in initiating indicated diagnostic and therapeutic measures in patients hospitalized in infirmaries, notably the initiation of broad-spectrum antibiotic therapy [15].

Cluster analysis revealed distinct patterns in the thermal evolution of the patients, demonstrating a statistically significant association between higher temperature curves, regardless of fever peaks, and the occurrence of infection. Although exploratory, this data suggests that the use of temperature trends,

and not mere values above the limits that define fever, may help to identify neutropenic patients with a higher chance of developing infectious complications. The same applies to other outcomes, given that patients in the group with higher temperatures throughout the monitoring period had longer hospital stays, transfers to ICUs, and deaths. Although they did not specifically investigate these associations, studies by (Palma et al. 2018; [16]) and (Drummond et al. 2020; [17]) highlighted the high accuracy of remote monitoring devices in measuring physiological parameters, corroborating the findings of the present study and emphasizing the positive impact of these technologies on the early detection of infections.

Although the benefits of continuous vital sign monitoring are evident, challenges such as adherence, usability, esthetics, and discomfort have been identified as potential barriers to implementation. More than half of the patients invited to participate in the study refused. However, the questionnaire applied to the included patients indicated that, despite discomfort related to the use of wires, fixation, and size of the equipment, most participants had a positive impression. The monitoring did not cause a negative impact, suggesting that the technology may be viable in routine hospital settings [18]. Smarr et al. (2022) [19], when evaluating a wearable ring for continuous temperature monitoring in individuals with COVID-19, also reported difficulties related to adherence and usability, such as the non-use of the device by some participants and inaccurate information provided by the participants themselves about their health status, and highlighted the need for technical improvements to ensure data reliability. In that study, optimization strategies led to substantial improvements in the accuracy and stability of temperature monitoring, thereby consolidating the clinical viability of the technology.

The findings obtained in this study reinforce the contribution of remote temperature monitoring systems to patient safety, as they enable the early detection of clinical changes and allow for faster and more effective interventions. The tested technology demonstrates the potential to optimize clinical decision-making, in turn reducing risks associated with treatment delays. In the same context, (Subbe et al. 2017; [20]), when implementing an automated vital sign monitoring and notification system, verified the positive impact on the early detection of clinical deterioration, increasing the activation of the rapid response team and allowing for more timely interventions. The monitoring model used in Subbe's study contributed to the reduction of mortality, cardiac arrests, and the severity of cases admitted to the ICU, reinforcing its effectiveness in improving clinical outcomes.

The main strengths of this study include its originality in evaluating the use of a non-invasive device for continuous temperature monitoring, specifically in neutropenic cancer patients hospitalized in an infirmary – a population highly vulnerable to infectious complications. The results demonstrated the feasibility of applying this technology in the hospital setting, highlighting its superiority in the early detection of fever as compared to routine care. Furthermore, the study identified an association between elevated temperature levels and worse clinical outcomes, such as a higher risk of sepsis, ICU admission, and death, emphasizing the potential of continuous monitoring to improve risk assessment and optimize the management of these patients.

Some limitations of this study should be considered. Monitoring was restricted to a single physiological parameter, without providing complementary information on other relevant vital signs, such as heart rate, respiratory rate, peripheral oximetry or blood pressure, which limits the use of the device as an early warning of clinical deterioration. Additionally, the high rate of refusal to participate in the study may indicate barriers related to discomfort with the continuous use of the device, privacy concerns, or a lack of familiarity with the technology. Furthermore, the exclusion of some participants who did not adhere to the use of the device represents a sample loss and may compromise the internal validity of the study and the generalizability of the findings. These events suggest the need to improve the device, making it fully wireless and miniaturized. Finally, the temperature data collected by the device being tested were compared with those obtained by the nursing staff in their routine care. Although there is a standardization of care at the hospital where the study was conducted, local care limitations (e.g., reduced staff, workload) may have influenced the results, increasing the difference found in favor of the remote device.

5. Conclusion

This study demonstrated that continuous temperature monitoring using a non-invasive device allows for the early detection of fever in neutropenic cancer patients, potentially anticipating the identification of infectious complications and reducing the time to institute diagnostic and therapeutic measures. Elevated temperature curves identified by continuous monitoring showed an association with worse clinical outcomes, reinforcing the usefulness of this technology in risk stratification. Although the findings are promising, challenges such as usability, adherence, and technical limitations still need to be overcome to enable its large-scale implementation. Future studies, with larger patient samples and monitoring of multiple vital signs, will be crucial to consolidating this approach in clinical practice and evaluating its impact on reducing serious complications.

Abbreviations

ICU
Intensive Care Units
HC-UFMG
Hospital das Clínicas of the Universidade Federal de Minas Gerais
COEP
Comitê de Ética e Pesquisa

Declarations

Ethics approval and consent to participate

The study was approved by the UFMG Ethics and Research Committee (*Comitê de Ética e Pesquisa* – COEP) (CAAE: 54215716.8.0000.5149) and Informed Consent Forms were offered to the research

participants who were included in the study.

Consent for publication

Not applicable.

Availability of data and materials

The data that has been used is confidential.

Competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' contributions

All authors — Isabella Santana dos Anjos, Pablo Gustavo Oliveira Silva, Andreza Werli, Isabella Rocha Soares, Paulo Henrique da Silva Menezes, Cecilia G. Ravetti, Ana Laura Grossi de Oliveira, and Vandack Nobre — actively participated in all stages of the article's development, including study conception and planning, testing, data collection, organisation, and analysis, interpretation of results, discussions, and literature review. All authors contributed to the writing and critical revision of the manuscript, participated in discussions and refinement of the scientific content, approved the final version of the article, and take responsibility for the content presented.

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Figures

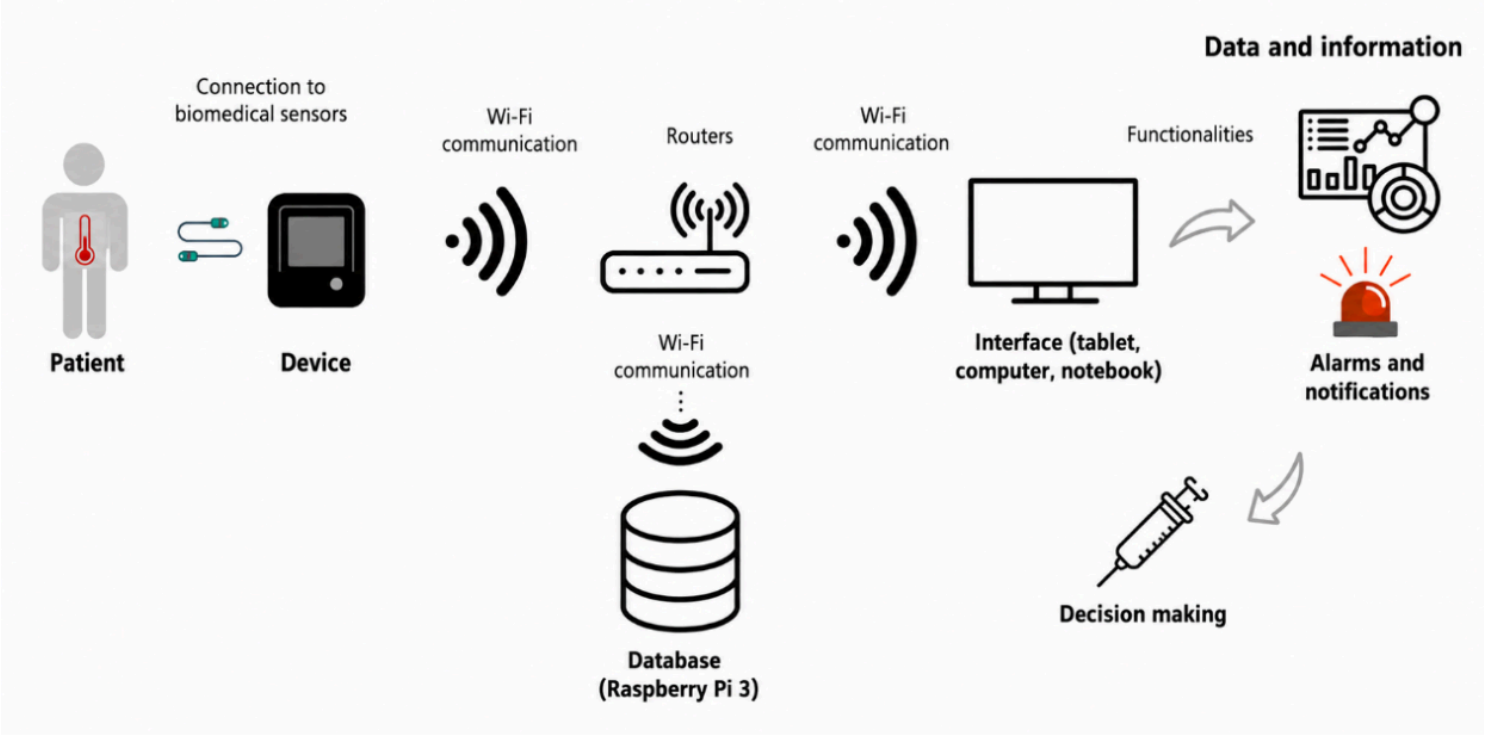

Figure 1

Data processing environment.

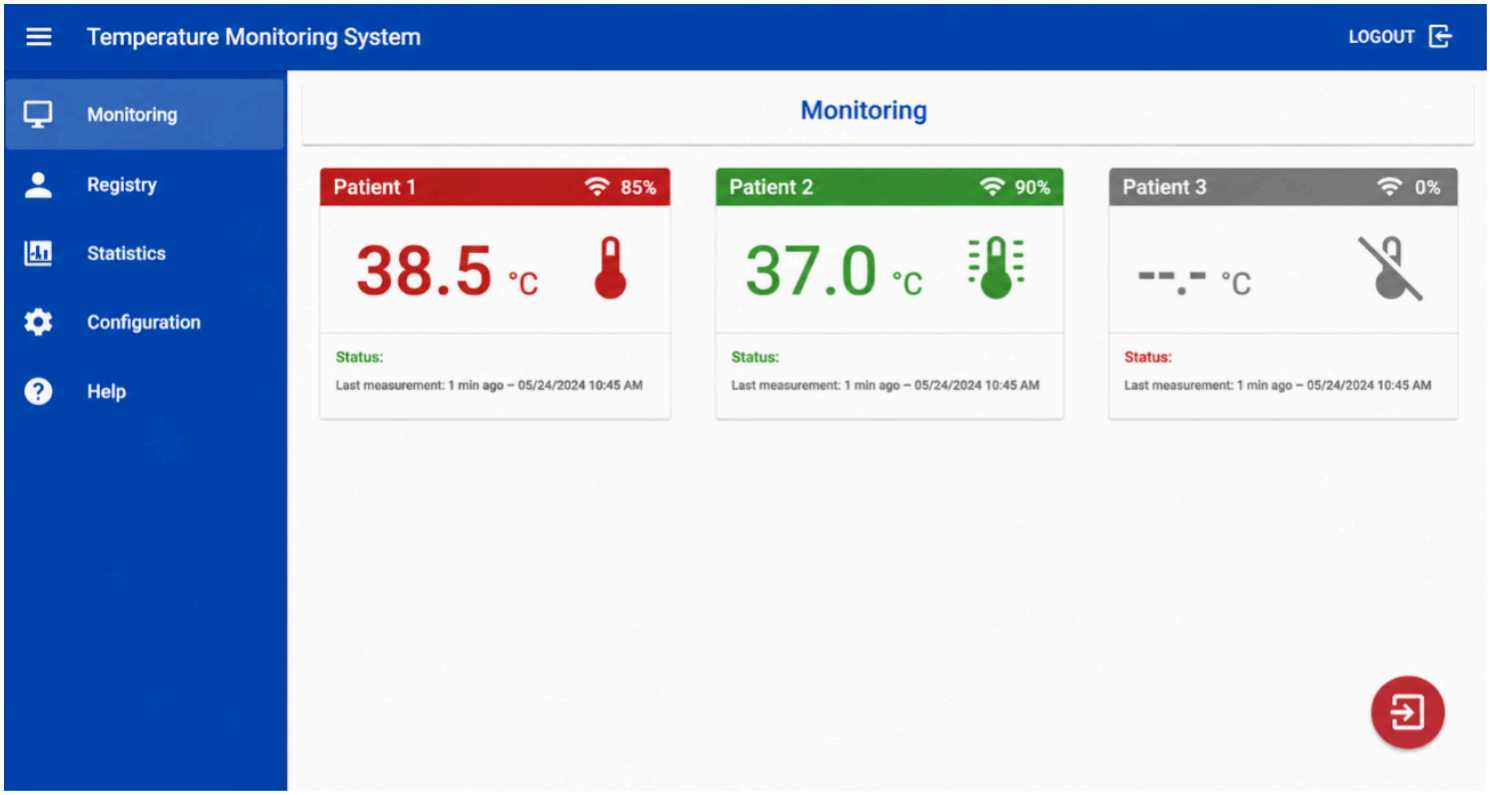

Figure 2

Device interface.

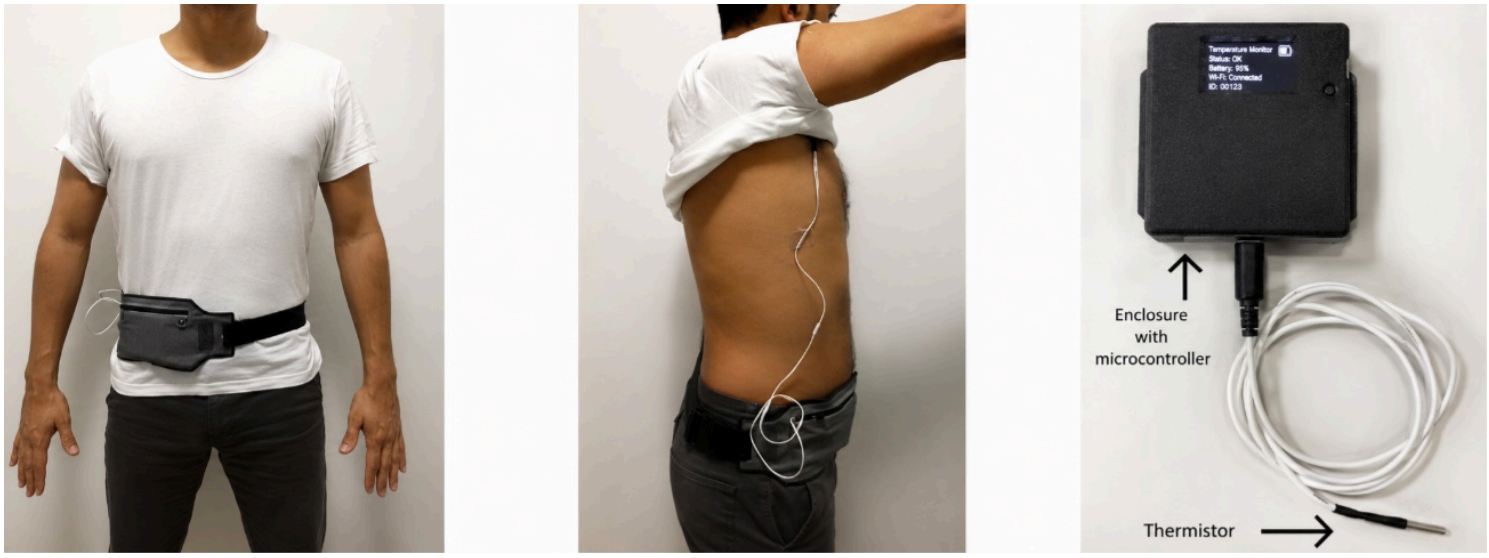

Figure 3

Healthy volunteer using the device

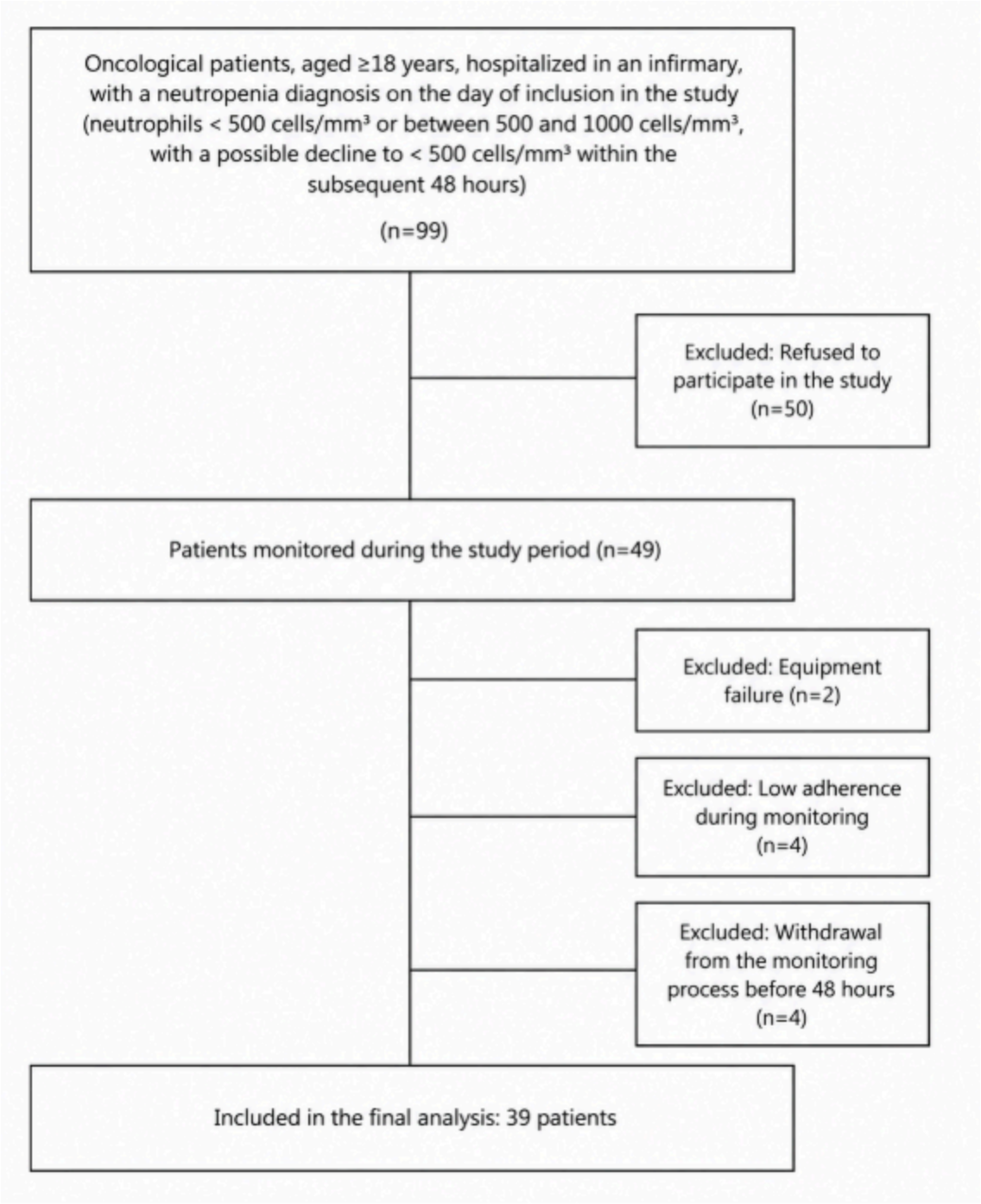

Figure 4

Flowchart of patient selection for the study according to inclusion and exclusion criteria.

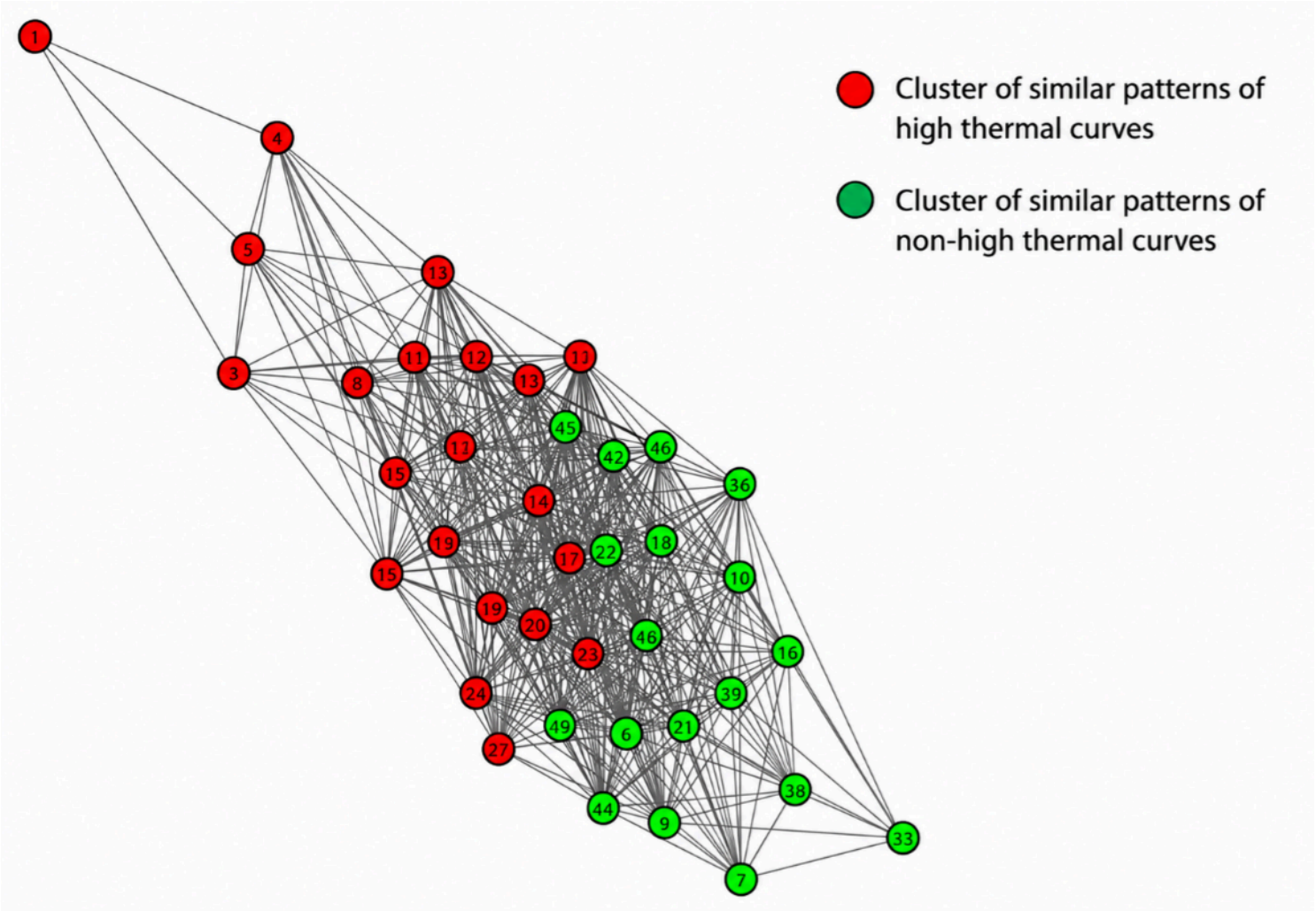

Figure 5

Grouping of Similar Thermal Patterns Based on Cluster Analysis using the Network Node Dispersion Technique.

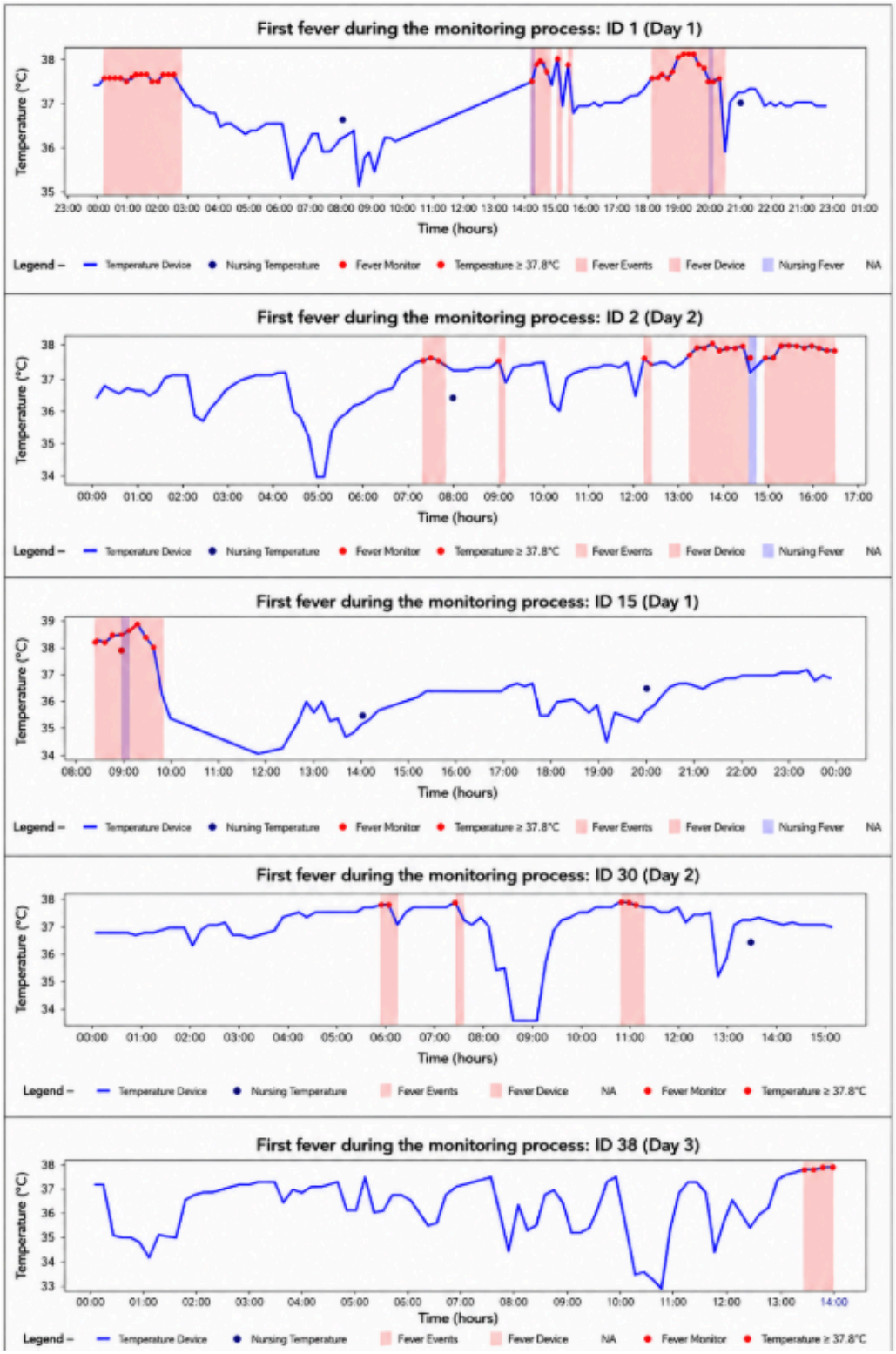

Figure 6

Graphs of the hourly temperature curve of the subgroup of patients with fever: comparison between monitoring by device and monitoring by the healthcare team.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMaterial.docx