Clinical Evaluation of Fever-Screening Thermography:
Impact of Consensus Guidelines and Facial Measurement Location

YANGLING ZHOU
   University of Maryland

PEJMAN GHASSEMI
   Food and Drug Administration

MICHELLE CHEN
   Johns Hopkins University

DAVID MCBRIDE
   University of Maryland

JON P. CASAMENTO
   Food and Drug Administration

T. JOSHUA PFEFER
   Food and Drug Administration

QUANZENG WANG (quanzeng.wang@fda.hhs.gov)
   Food and Drug Administration

Research Article

Keywords: fever screening, thermography, medical guidelines, inner canthi, infectious disease epidemics, COVID-19, receiver operating characteristic, Pearson correlation coefficients, thermometry, facial maximum temperatures

DOI: https://doi.org/10.21203/rs.3.rs-28139/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Infrared thermographs (IRTs) have been used for fever screening during infectious disease epidemics, including SARS, EVD and COVID-19. Although IRTs have significant potential for human body temperature measurement, the literature indicates inconsistent diagnostic performance, possibly due to wide variations in implemented methodology. A standardized method for IRT fever screening was recently published, but there is a lack of clinical data demonstrating its impact on IRT performance. We have performed a clinical study of 596 subjects to assess the diagnostic effectiveness of standardized IRT-based fever screening and evaluate the effect of facial measurement location. Temperatures from 17 facial locations were extracted from thermal images and compared with oral thermometry. Statistical analyses included calculation of receiver operating characteristic curves and area under the curve (AUC) values for detection of febrile subjects. Pearson correlation coefficients for IRT-based and reference temperatures were found to vary strongly with measurement location. Approaches based on maximum temperatures in either inner canthi or full-face regions indicated stronger discrimination ability than maximum forehead temperature (AUC values of 0.95-0.97 vs. 0.86-0.87, respectively) and other specific facial locations. These values are markedly better than the vast majority of results from prior human studies of IRT-based fever screening. Thus, our findings provide clinical confirmation of the utility of consensus approaches for fever screening, including the use of inner canthi temperatures, while also indicating that full-face maximum temperatures may provide an effective alternate approach.

1. Introduction

Fever is a key symptom of infectious diseases that have caused epidemics such as Severe Acute Respiratory Syndrome (SARS) in 2003, influenza A (H1N1) in 2009, Ebola virus disease (EVD) in 2014 and coronavirus (COVID-19) in 2020\(^1\)-\(^6\). Fever screening is a medical countermeasure used at international borders, public transportation hubs and hospitals to mitigate the propagation of these diseases. Often, a diagnostic based on radiative heat transfer from the human body (\textit{i.e.}, infrared technology) is used for primary screening in combination with other approaches, such as symptom questionnaires\(^3\),\(^7\),\(^8\). If the subject is determined to be positive in primary screening, a secondary screening may be implemented including contact measurements (\textit{e.g.}, oral thermometry) and/or sampling for a laboratory test.

Non-contact infrared thermometers (NCITs)\(^9\),\(^10\) and infrared thermographs (IRTs)\(^11\) represent the primary device types currently used in practice for real-time screening of infectious disease during epidemics. NCITs and IRTs are passive remote sensing devices that detect mid- and/or long-wave infrared (IR) radiation and convert that radiation to temperature based on the Stefan-Boltzmann law\(^12\). NCITs estimate temperature at a reference body site (usually oral) based on measurements of a single region of skin (\textit{e.g.}, forehead)\(^13\), whereas IRTs provide a 2D temperature distribution – typically of the face – thus enabling a wider range of options for body temperature estimation. Although NCITs currently represent the primary tool for fever screening during epidemics\(^14\), their accuracy has been called into question, particularly relative to IRTs\(^15\),\(^16\). NCIT error may be due to a range of factors including the common use of forehead measurement locations, which are subject to fluctuations due to environmental factors like ambient temperature and air flow\(^7\).
Human subject studies have demonstrated that IRTs can estimate body temperature and detect febrile individuals with moderately high accuracy. Several studies on IRT-based fever detection screening in hospital settings found "optimal" sensitivity (Se) and specificity (Sp) values – the point on the receiver operator characteristic (ROC) curve where both Se and Sp are high – in the 0.70-0.80 range\(^\text{15,17,18}\). Hewlett et al. studied patients arriving at a hospital during the 2009 H1N1 influenza pandemic and found Se/Sp of 0.70/0.92 (area under the curve, AUC = 0.86) for IRT-identified subjects with fever above 100 °F (37.8 °C), although no data was provided on detection of subjects infected with H1N1 influenza\(^\text{19}\). One study performed in an airport also indicated similar Se/Sp levels, yet identified a minimal number of infected travelers\(^\text{20}\); this result was attributed to a lack of high fevers in the infected travelers identified. Similarly, in another airport screening study, Cho et al. were only able to detect 6 febrile travelers out of over 350,000 screened\(^\text{21}\). This lack of sensitivity may have been due in part to using a wide-field screening approach rather than the single-subject approach implemented in most of the aforementioned studies. In an extensive review of screening procedures during infectious disease epidemics, Mouchtouri et al.\(^\text{22}\), indicated that thermal diagnostics can be somewhat effective, yet often require great resource expenditures (\emph{e.g.}, device cost, personnel), and in the case of some epidemics like SARS, their practical impact may be minimal. However, this review did not address variations in IRT device quality and implementation, which are likely significant factors in determining real-world effectiveness\(^\text{23,24}\).

Improvements in IRT-based temperature measurement accuracy could enable detection of lower grade fevers (\emph{e.g.}, 37-38 °C). Such temperatures may be associated with early disease stages, such when symptoms are starting to become evident in COVID-19\(^\text{25}\) and viral shedding is particularly high\(^\text{26}\). This capability may be particularly relevant to transportation and containment, since individuals with fully developed symptoms may remain home or seek medical care, whereas those with less severe symptoms are more likely to travel. Furthermore, in diseases with significant person-to-person variations in symptom intensity, fully developed illness with low grade fever would be more common. Alternately, enhanced IRT system accuracy could enable improved Se or Sp for high grade fever, thus reducing the large number of false positives that are likely due to the high prevalence of afebrile individuals and wide variations in normal temperatures\(^\text{27}\) or slightly improving the likelihood of detected infected individuals.

Optimizing IRT-based screening requires consideration of fundamental device performance, implementation practices and confounding factors such as environmental conditions. With the steady increase in use of IRTs for medical applications, consensus documents for IRT evaluation and application have recently been published. International standard IEC 80601-2-59:2017\(^\text{23}\) provides recommendations for performance characterization of fever-screening IRTs. In a prior study, we implemented and evaluated these recommendations using two commercial IRTs\(^\text{28}\), but we are not aware of any prior IRT clinical study which has implemented this standard. A consensus technical report, ISO/TR 13154:2017\(^\text{24}\), describes best practices for IRT deployment, implementation and operation. These include approaches that have not been commonly employed during disease epidemics, such as including a high-quality blackbody in the thermal image to minimize the impact of environmental factors as well as IRT instability and drift. This report also recommends measurements be performed on individuals rather than a crowd, and that the inner canthus (tear duct) regions be measured in order to reduce measurement variability.
IRTs measure body surface temperatures that can be calibrated to or matched with corresponding oral or tympanic temperatures, which provide optimal discrimination based on ROC curve analysis. While some prior studies have equated oral and tympanic temperatures with core temperature, it is more accurate to say that these internal, yet accessible sites act as well-correlated surrogates for core temperature. In IRT images, a variety of facial measurement locations and processing methods have been investigated to optimize IRT fever screening performance. The inner canthi are thought to be an ideal location for non-contact temperature measurements. Perfused by the internal carotid artery, they have high temperature stability, are typically the warmest regions on the face, and have the highest correlation with internal body temperature. However, another study concluded that the correlation between ear (contact) and eye (non-contact) temperature was lower than expected. The maximum temperature around the eyes has also been studied. Several other IRT measurement regions have been evaluated, including the entire face, temples, nose, cheeks, ear, mouth (open and closed), and the forehead. From these previous studies, it is difficult to draw a clear conclusion regarding the optimal approach for temperature measurement from IRT images.

The purpose of this study was to generate independent data to assess the potential of IRTs for fever screening when implemented according to international consensus documents, while also elucidating the impact of facial measurement location and other key issues on IRT-based fever screening performance. Specifically, our goals included: (a) acquisition of clinical IRT and reference temperature data in a large population of febrile and non-febrile subjects using standardized methods; (b) evaluation of facial measurement locations for their impact on correlation to – and absolute agreement with – oral temperature; and (c) comparative statistical analysis of febrile subject detection performance using these methods.

2. Methods

Over the course of 18 months – from November 2016 to May 2018 – we conducted a clinical study of 596 subjects at the Health Center of the University of Maryland (UMD) at College Park. Both FDA and UMD Institutional Review Boards (IRBs) approved this study under FDA IRB study #16-011R and written informed consent was obtained from all subjects. All experiments were performed in accordance with relevant guidelines and regulations. Informed consent has been obtained for publishing recognizable images in this paper. The screening area was prepared according to consensus document specifications. Measurements of study subjects were performed with an oral thermometer, multiple NCITs and two IRTs. The NCIT data and analysis will be the subject of a future paper. As detailed below, the current work focuses on analysis of a subset of the measurements acquired for each subject.

2.1 Experimental setup and temperature measurement

As noted in ISO/TR 13154 and IEC 80601-2-59, a screening thermograph system includes an IRT and an external temperature reference source, or blackbody. The reference source should have a known radiance temperature (function of real temperature and emissivity, ε) over the range of 33°C to 40°C with an expanded uncertainty (coverage factor of 2 for a ~95% level of confidence) of ± 0.3°C or less and a combined stability and drift of ± 0.1°C over the temperature interval for measurement, and its image size...
should be greater than or equal to 20×20 pixels. A workable target plane (WTP) is a specific region of the target plane that is used for temperature measurement; it should accommodate a subject's face positioning from 0.75 to 2.2 meters above the floor. The WTP image pixel size should be at least 320×240. For ambient conditions, the temperature should be 18-24°C and relative humidity should be 10-75%. Forced cooling or heating of the target due to airflow or lighting should be avoided or at least minimized.

Based on ISOTR 13154 recommendations, a screening room was established as illustrated in Figure 1. The setup consisted of a webcam (C920, Logitech, Lausanne, Switzerland) and two IRTs (IRT-1: 320×240 pixels, A325sc, FLIR Systems Inc., Nashua, NH; IRT-2: 640×512 pixels, 8640 P-series, Infrared Cameras Inc., Beaumont, TX) that were mounted in adjacent positions on a tripod. A WTP with dimensions of 320×240 pixels was identified for each IRT – the entire image for IRT-1 and a subset of the image in the most uniform region for IRT-2. We developed a graphical user interface (GUI) with MATLAB to simultaneously control the webcam and two IRTs, as well as to collect images and patient/environmental information. Both IRTs had 30 Hz frame rates, and detailed specifications and fundamental performance testing results can be found in our prior study. A blackbody (SR-33, CI Systems Inc.) with a 4 × 4 inch emitter (image size > 20 × 20 pixels) was set at 35°C then positioned perpendicular to the sight line of the cameras and placed within the frame alongside the subject’s face for temperature drift compensation. We previously verified that blackbody drift and uncertainty satisfied relevant standards. The subject-to-camera distance was 0.6-0.8 meters to ensure that both the subject's face and the blackbody were included in the WTP with a resolution that satisfied recommended specifications. Room temperature was maintained between 20°C and 24°C and relative humidity between 10% and 62%, as measured by a weather tracker (Kestrel 4500 NV, Weather Republic LLC, Downingtown, PA). Ambient temperature and subject ε (0.98 for human skin) were entered into the IRT control program as input parameters for calibrating measured temperature. To prevent direct airflow to a subject's face, an air vent in the room was blocked by a magnetic air deflector. A black, low-reflectivity cloth (ε=0.97; Type 822 E0.97, Group 8 technology, Provo, UT) was used as the backdrop.

To minimize the influence of outside temperature, each subject was instructed to wait for 15 minutes before measurements started. Once seated, the subject was asked to remove all obstructions from the face (e.g., eyeglasses and hair on forehead) and look at the IRTs. Then, the tripod was adjusted to center the subject’s face in the cameras’ fields of view. For each subject, four rounds of measurements were performed within ~25 minutes, following the procedure shown in Figure 2. In each round, temperatures were measured with two IRTs (facial images) and several NCITs (forehead temperature). NCIT measurements performed in this study are beyond the scope of the current paper but are under analysis for a future publication.

During each round of imaging, the webcam acquired one standard color image, while each IRT acquired three consecutive frames (acquisition time ~ 0.1 sec) that were averaged to reduce noise and form a single mean thermal image. In the last round, the subject was instructed to open their mouth to enable thermal imaging of sublingual tissue. Images from the second to fourth rounds of measurements were omitted in the current analysis, to better approximate a realistic screening scenario, but will be evaluated in a future study.
Oral thermometry was used to establish reference temperatures\textsuperscript{32}. A thermometer (SureTemp Plus 690, Welch Allyn, San Diego, CA) was placed under the subject’s tongue in a sublingual pocket (heat pocket). Then the temperature was read in two different modes, a “fast” mode in several seconds and a “monitor” mode after three minutes. Fast mode data were not used in this study due to insufficient accuracy. The monitor mode has accuracy of ±0.1 °C, which was confirmed against a NIST-traceable contact thermometer (6413, Traceable® Products, Webster, TX) using a laboratory water bath (89202-926, VWR International, Radnor, PA). The reference temperature ($T_{\text{ref}}$) was calculated as the mean of two oral temperature measurements in monitor mode (during rounds 1 and 3). All subject data were discarded if the difference between two readings was larger than 0.5 °C, due to the likelihood of a measurement error.

2.2 Facial region delineation and temperature measurement

Temperatures from several facial areas – including the forehead, canthi, mouth and entire face – were compared to assess impact on fever screening (Figure 3). Standards documents do not specify a method for delineating facial key-points such as canthi in IRT images, so we implemented an image registration approach\textsuperscript{37} to identify these points by matching facial landmarks on visible light images to IRT images. However, key-points for about half of these images required manual labeling. Based on the identified facial key-points, different regions/points on thermal images were defined (Figure 3).

As shown in Figure 3, the extended forehead area was determined in the vertical direction by hairline and eyebrows. The maximum single-pixel temperature in the extended forehead area ($T_{FE\text{max}}$) was first obtained. Then, the center forehead area was defined in the horizontal direction by the canthus points and in the vertical direction by 70% of the height of the forehead area from the bottom edge (eyebrows), and its maximum temperature ($T_{FC\text{max}}$) was obtained. Five points were defined in the forehead center region rectangle – the center point and the middle points of the top, bottom, left and right edges. At each of these points, the mean temperature of a 3 × 3 pixel region was used to determine results ($T_{FC}$, $T_{FT}$, $T_{FB}$, $T_{FL}$ and $T_{FR}$).

Two inner canthus points were identified in each IRT image using the registration method\textsuperscript{37}. Two small circular regions of interest (ROIs) were defined with a diameter of 13 pixels, using the inner canthus points as their outer edge. The mean and maximum temperatures of the left ($T_{CL}$ and $T_{CL\text{max}}$) and right ($T_{CR}$ and $T_{CR\text{max}}$) ROIs were obtained. From these values, the mean and maximum of $T_{CL}$ and $T_{CR}$ ($T_C$ and $T_{C\text{max}}$) and the maximum of $T_{CL\text{max}}$ and $T_{CR\text{max}}$ ($T_{C\text{max}2}$) were also calculated. An extended canthus region was delineated, which was centered at the two canthus points and having a width of 96 pixels. Its top edge extended upwards to the bottom of the eyebrows, and its bottom edge extended downwards by the same amount. The maximum temperature ($T_{CE\text{max}}$) of this area was obtained.

The mouth region was defined by a rectangle that included all the facial key-points around the mouth, then the maximum temperature of this region ($T_{M\text{max}}$) was identified. The entire face region was defined horizontally by the edges of the face and in the vertical direction by the chin and hairline, and its maximum temperature was determined ($T_{max}$).
2.3 Data analysis

2.3.1 Temperature compensation

Since IRTs exhibit varying degrees of instability and drift, a blackbody was used for thermal image compensation. By comparing the IRT-measured blackbody temperature ($T_{B\text{meas}}$) with its set temperature ($T_{B\text{set}}$) of 35°C, we identified an appropriate offset for each image. Specifically, the equation $T_{\text{off}} = T_{B\text{set}} - T_{B\text{meas}}$ was used, where $T_{\text{off}}$ is the offset value added to every pixel in the image. Unless otherwise specified, all data in this paper were compensated with the blackbody in this manner.

2.3.2 Statistical analysis

To assess the effect of facial location for fever screening, results were analyzed using comparative boxplots, scatter plots, correlation coefficients, and receiver operating characteristic (ROC) curves. Temperatures obtained from IRT images were compared with the reference temperature ($T_{\text{ref}}$). The pairwise difference between $T_{\text{ref}}$ and temperatures extracted from different facial locations ($T_{\text{IRT}}$) was obtained. Comparative boxplots were used to display and compare pairwise differences. The Pearson correlation coefficient ($r$ value) was used to quantify the degree of linear correlation between $T_{\text{IRT}}$ and $T_{\text{ref}}$.

ROC curves – which plot sensitivity (Se, true positive rate) vs. 1-specificity (Sp, true negative rate) for a range of cut-off levels – were used to assess discrimination between febrile and afebrile subjects. True febrile status was defined as $T_{\text{ref}} \geq 37.5^\circ\text{C}$\textsuperscript{20,39,40}. An ROC curve for each facial temperature location was generated from 1000 IRT-based cut-off temperatures equally spaced between 30°C and 40°C. At each cut-off temperature, the numbers of positive and negative subjects – and thus pairs of Se/Sp values – were determined based on true febrile status. The area under the ROC curve (AUC) was calculated to provide an aggregate measure of performance (where an AUC of 1.0 indicates perfect diagnostic performance). AUC values for different facial temperatures were compared using pairwise tests with a 95% confidence interval (Analyse-it, Method validation edition, Analyse-it Software, Ltd., Leeds, UK). For each ROC curve, the optimal IRT cut-off temperature was determined as either the point on the ROC curve closest to (0, 1)\textsuperscript{38} or the Youden index\textsuperscript{41}. As both methods yielded very similar results, we only used the former method to find the optimal cut-off temperature which minimizes the quantity $[(1-\text{Se})^2 + (1-\text{Sp})^2]$ and thus yields the greatest combined sensitivity and specificity.

3. Results

3.1 Subject demographics

A total of 596 subjects were recruited; all were at least 18 years old and free of disease affecting the skin in canthi area or forehead one week prior to the screening date. Among these subjects, 33 had two oral temperature readings with difference greater than 0.5°C, and thus were removed from the database. Of the remaining 563 sets of subject data, we excluded 19 from IRT-1 and 23 from IRT-2 due to motion artifacts.
that degraded image quality. Finally, we had 544 data sets for IRT-1 and 540 data sets for IRT-2.

Demographic information for study subjects is summarized in Table 1.

|                | IRT-1 |      | IRT-2 |      |
|----------------|-------|------|-------|------|
|                | Subjects | %     | Subjects | %     |
| Female         | 329    | 60.5 | 328    | 60.7 |
| Male           | 215    | 39.5 | 212    | 39.3 |
| Age 18-20      | 263    | 48.3 | 262    | 48.5 |
| Age 21-30      | 247    | 45.4 | 0      | 0.0  |
| Age 31-40      | 21     | 3.9  | 21     | 3.9  |
| Age 41-50      | 4      | 0.7  | 4      | 0.7  |
| Age 51-60      | 7      | 1.3  | 7      | 1.3  |
| Age >60        | 2      | 0.4  | 2      | 0.4  |
| Ethnicity      |        |      |        |      |
| White          | 257    | 47.2 | 254    | 47.0 |
| Black/African-American | 78 | 14.3 | 79 | 14.6 |
| Hispanic/Latino | 39 | 7.2  | 39 | 7.2  |
| Asian          | 138    | 25.4 | 136    | 25.2 |
| Multiracial    | 30     | 5.5  | 30     | 5.6  |
| American Indian | 2   | 0.4  | 2      | 0.4  |
| $T_{ref} > 37.5^\circ C$ | 47 | 8.6  | 47 | 8.7  |

3.2 Temperature measurement accuracy and correlation

Temperatures for different facial locations from thermal images were compared with $T_{ref}$. For each IRT, comparative boxplots of pairwise differences with $T_{ref}$ were constructed (Figure 4). For all temperatures from both IRTs, pairwise differences were positive. This is consistent with prior studies, and expected given that sublingual tissue is not typically subjected to the levels of convective heat loss that external tissues experience. Overall, the forehead region showed the greatest discrepancy, then the canthus regions, and the entire face maximum shows the least difference.

| Forehead        | Inner canthi | Mouth | Face |
|-----------------|--------------|-------|------|
| $T_{FC}$        | $T_{FT}$     | $T_{FB}$ | $T_{FL}$ |
| $T_{FC_{max}}$  | $T_{FT_{max}}$ | $T_{FB_{max}}$ | $T_{FL_{max}}$ |
| $T_{LC}$        | $T_{CR}$     | $T_{C_{max1}}$ | $T_{C_{max2}}$ |
| $T_{LC_{max}}$  | $T_{CR_{max}}$ | $T_{C_{max1_{max}}}$ | $T_{C_{max2_{max}}}$ |
| $T_{max}$       | $T_{max}$    | $T_{max}$ | $T_{max}$ |
| IRT-1           | 0.46, 0.41, 0.49, 0.47, 0.43, 0.55, 0.63, 0.60, 0.58, 0.63, 0.65, 0.70, 0.71, 0.73, 0.75, 0.60, 0.78 |
| IRT-2           | 0.46, 0.39, 0.49, 0.46, 0.41, 0.54, 0.62, 0.53, 0.51, 0.56, 0.59, 0.70, 0.69, 0.73, 0.76, 0.60, 0.79 |

Pearson correlation coefficients for all measurement locations were highly consistent with the pairwise difference results. Among the seven forehead temperatures, $r$ values varied from 0.39 to 0.63 with $T_{F_{max}}$ showing the highest correlation and agreement with $T_{ref}$, followed by $T_{C_{max}}$. The maximum temperature around the mouth ($T_{M_{max}}$) showed results that were similar to $T_{F_{max}}$. Correlation results for inner canthi temperatures were in general higher than for the forehead, ranging from 0.51 to 0.76. The highest $r$ values (>0.7) were found for maximum temperatures across left and right inner canthi regions ($T_{C_{max2}}$), the extended inner canthi region ($T_{C_{E_{max}}}$), and the entire face ($T_{max}$). As $T_{max}$ had the largest $r$ value, this metric may best estimate $T_{ref}$. 
Facial temperature correlations were further analyzed with scatter plots of $T_{IRT}$ versus $T_{ref}$ for select facial locations (Figure 5). These included $T_{Cmax1}$, which aligns with IEC TR 13154 recommendations (although this approach is not explicitly defined), as well as $T_{FEmax}$, $T_{CEmax}$ and $T_{max}$, which showed the best $r$ values for extended forehead, extended inner canthi and whole face regions, respectively. As expected, scatter plots show a large grouping of $T_{ref}$ values near 37 °C, representing the high proportion of afebrile subjects (84% of $T_{ref}$ readings were between 36.4 – 37.4 °C). $T_{Cmax1}$ results showed the greatest variability, most notably in the sub-febrile range. $T_{FEmax}$ results showed improved correlation with $T_{ref}$ in this range, as well as across higher $T_{ref}$ values. $T_{CEmax}$ and $T_{max}$ measurements were less variable than other measurements and well-correlated to $T_{ref}$, approaching a linear relationship. Data for the two IRT systems showed only minor differences in correlation.

### 3.3 Fever detection performance

ROC curve analysis was used to evaluate performance of IRT-based detection of febrile subjects and its dependence on facial measurement location. Figure 6 shows ROC curves for $T_{Cmax1}$, $T_{FEmax}$, $T_{CEmax}$ and $T_{max}$, while AUC values for all measurements are found in Table 3. In Figure 6, the $y = x$ line denotes random discrimination; all ROC curves from our study were well above this line. $T_{max}$ and $T_{CEmax}$ yielded optimal ROC curves with AUC values $> 0.95$, indicating high discrimination effectiveness. IRT-2 showed slightly better performance for $T_{max}$ than $T_{CEmax}$. ROC curves for $T_{Cmax1}$ and $T_{FEmax}$ indicated lower performance, with the most notable feature being a slow convergence to high sensitivity as specificity decreased. In general, discrimination performance for $T_{IRT}$ aligned well with correlations to $T_{ref}$ shown in (Table 2).

#### Table 3 AUC values from the ROC curves for different facial locations

| Forehead | Inner canthi | Mouth | Face |
|----------|-------------|-------|------|
| $T_{FC}$ | $T_{FT}$ | $T_{FB}$ | $T_{FF}$ | $T_{FR}$ | $T_{Cmax}$ | $T_{FEmax}$ | $T_{CL}$ | $T_{CR}$ | $T_{Cmax1}$ | $T_{Cmax2}$ | $T_{max}$ | $T_{Cmax}$ | $T_{Cmax}$ | $T_{max}$ |
| IRT-1 | 0.82 | 0.79 | 0.82 | 0.80 | 0.81 | 0.84 | 0.86 | 0.88 | 0.87 | 0.88 | 0.94 | 0.93 | 0.94 | 0.95 | 0.89 | 0.95 |
| IRT-2 | 0.82 | 0.79 | 0.82 | 0.79 | 0.79 | 0.84 | 0.87 | 0.91 | 0.87 | 0.90 | 0.92 | 0.95 | 0.93 | 0.94 | 0.95 | 0.88 | 0.97 |

#### Table 4 Results of pairwise comparisons of the AUC values for $T_{max}$, $T_{CEmax}$ $T_{FEmax}$ and $T_{Cmax1}$. Bold values indicate $p > 0.05$. 

Data for the two IRT systems showed only minor differences in correlation.

3.3 Fever detection performance

ROC curve analysis was used to evaluate performance of IRT-based detection of febrile subjects and its dependence on facial measurement location. Figure 6 shows ROC curves for $T_{Cmax1}$, $T_{FEmax}$, $T_{CEmax}$ and $T_{max}$, while AUC values for all measurements are found in Table 3. In Figure 6, the $y = x$ line denotes random discrimination; all ROC curves from our study were well above this line. $T_{max}$ and $T_{CEmax}$ yielded optimal ROC curves with AUC values $> 0.95$, indicating high discrimination effectiveness. IRT-2 showed slightly better performance for $T_{max}$ than $T_{CEmax}$. ROC curves for $T_{Cmax1}$ and $T_{FEmax}$ indicated lower performance, with the most notable feature being a slow convergence to high sensitivity as specificity decreased. In general, discrimination performance for $T_{IRT}$ aligned well with correlations to $T_{ref}$ shown in (Table 2).
The statistical significance of AUC differences between $T_{C_{max1}}, T_{F_{E_{max}}, T_{C_{E_{max}}}$ and $T_{max}$ was evaluated using six pairwise tests (Table 4). For both IRTs, there was no statistically significant difference ($p \geq 0.05$) between AUC values of $T_{max}$ and $T_{C_{E_{max}}}$, and these parameters were both significantly higher ($p < 0.05$) than $T_{F_{E_{max}}}$ . When compared to $T_{C_{max1}}, T_{max}$ showed a significantly higher AUC, but $T_{C_{E_{max}}}$ showed a significantly greater result for only one of the two IRTs. Overall, this AUC comparison indicated that $T_{max}$ and $T_{C_{E_{max}}}$ should provide the most optimal results when used for fever screening.

Facial temperatures measured by IRTs are typically at least 1-2 °C lower than $T_{ref}^{34}$. Therefore, it is necessary to either calibrate $T_{IRT}$ to $T_{ref}$ or find a suitable cut-off temperature for each IRT during fever screening. For consistency with prior IRT studies $^{18,20}$, we used the latter method. Our results above (Figure 6, Table 4) were based on defining fever as $T_{ref} \geq 37.5^\circ C$, from which an optimal cut-off temperature can be obtained for each IRT (first row in Table 5, Table 6 and Table 7). We also calculated the optimal cut-off temperature under diagnostic thresholds of 37.8 and 38.0 °C.

According to our results, $T_{max}$ and $T_{C_{E_{max}}}$ provided the best approaches for fever detection and did not exhibit significant differences in performance. However, the approach that most closely adheres to the recommendations in TR 13154 is $T_{C_{max1}}$. Therefore, we used all three temperatures in evaluating the optimal Se and Sp for different $T_{ref}$ diagnostic thresholds in Table 5, Table 6 and Table 7. Cut-off temperatures were calculated to optimize Se and Sp simultaneously $^{38}$.

| Oral thermometer | IRT-1 | IRT-2 |
|------------------|-------|-------|
| $T_{ref}$ diagnostic thresholds (°C) | Actual febrile # | IRT cut-off temperature (°C) | Se  | Sp  | Actual febrile # | IRT cut-off temperature (°C) | Se  | Sp  |
| 37.5  | 47   | 36.19 | 0.85 | 0.94 | 47   | 36.11 | 0.94 | 0.89 |
| 37.8  | 30   | 36.28 | 0.93 | 0.94 | 30   | 36.38 | 0.93 | 0.95 |
| 38.0  | 19   | 36.29 | 1.00 | 0.93 | 19   | 36.87 | 1.00 | 0.98 |

Table 5 Optimal IRT cut-off temperatures and related Se/Sp values for $T_{max}$ under different $T_{ref}$ thresholds
Table 6: Optimal IRT cut-off temperatures and related Se/Sp values for TCEmax under different Tref thresholds

| Oral thermometer | IRT-1 | | | IRT-2 | | |
|------------------|-------|---|---|-------|---|---|
| Tref diagnostic thresholds (°C) | Actual febrile # | IRT cut-off temperature (°C) | Se | Sp | Actual febrile # | IRT cut-off temperature (°C) | Se | Sp |
| 37.5 | 47 | 35.96 | 0.89 | 0.87 | 47 | 36.11 | 0.87 | 0.92 |
| 37.8 | 30 | 36.05 | 0.93 | 0.90 | 30 | 36.25 | 0.93 | 0.95 |
| 38.0 | 19 | 36.28 | 1.00 | 0.95 | 19 | 36.58 | 1.00 | 0.97 |

Table 7: Optimal IRT cut-off temperatures and related Se/Sp values for TCmax I under different Tref thresholds

| Oral thermometer | IRT-1 | | | IRT-2 | | |
|------------------|-------|---|---|-------|---|---|
| Tref diagnostic thresholds (°C) | Actual febrile # | IRT cut-off temperature (°C) | Se | Sp | Actual febrile # | IRT cut-off temperature (°C) | Se | Sp |
| 37.5 | 47 | 35.22 | 0.85 | 0.79 | 47 | 35.37 | 0.83 | 0.88 |
| 37.8 | 30 | 35.32 | 0.80 | 0.84 | 30 | 35.41 | 0.87 | 0.87 |
| 38.0 | 19 | 35.76 | 0.84 | 0.96 | 19 | 35.94 | 0.89 | 0.97 |

These results further illustrate how diagnostic performance decreased from Tmax to TCEmax to TCmax1. The Se/Sp values for Tmax and TCEmax are similar, which reflects the extent of overlap in their ROC curves (Figure 6) and minimal AUC differences (Table 4). Performance was good for TCmax1, yet significantly lower than for Tmax and TCEmax. While discrimination of febrile subjects was superior for a cut-off threshold of 38 °C, impressive outcomes were also obtained for lower grade fever thresholds at 37.5 °C and 37.8 °C. The trend of increasing Se/Sp with diagnostic threshold may be due to a larger difference between the temperature of febrile subjects and the normal temperature value where most of the subjects were; a normal temperature with some error is less likely to reach 38 °C.

3.4 Blackbody compensation

Temperature compensation using a validated blackbody (BB) was recommended by IEC TR 13154 to improve IRT system stability. To quantify the impact of this compensation, correlation coefficients between the facial temperatures and Tref (Table 8) and the AUC values based on a diagnostic threshold of 37.5 °C (Table 9) were calculated without BB compensation. Comparison of Table 2 with Table 8 show that the r values increased for all facial temperatures measured by both IRTs. The increases for TCmax1, TFEmax, TCEmax and Tmax are 7%, 13%, 13% and 12% for IRT-1 and 5%, 4%, 6% and 5% for IRT-2. Comparison of Table 3 with Table 9 show that the AUC values also increased for all facial temperatures. The increases for TCmax1, TFEmax, TCEmax and Tmax are 2%, 3%, 4% and 4% for IRT-1 and 2%, 1%, 3% and 3% for IRT-2.

Table 8: Pearson correlation coefficients (r values) between facial temperatures and Tref (no BB compensation)

| | Forehead | | | Inner canthi | | | Mouth | Face |
|---|---|---|---|---|---|---|---|---|
| | TFC | TFT | TFB | TFL | TFR | TFCmax | TFEmax | TCL | TCR | TC | TCmax1 | TCLmax | TCRmax | TCmax2 | CEmax | TMmax | Tmax |
| IRT-1 | 0.44 | 0.41 | 0.47 | 0.46 | 0.42 | 0.50 | 0.55 | 0.57 | 0.57 | 0.60 | 0.60 | 0.64 | 0.65 | 0.66 | 0.67 | 0.59 | 0.70 |
| IRT-2 | 0.45 | 0.38 | 0.48 | 0.45 | 0.39 | 0.52 | 0.60 | 0.51 | 0.48 | 0.53 | 0.56 | 0.67 | 0.66 | 0.69 | 0.71 | 0.58 | 0.75 |
Table 9 AUC values from the ROC curves of different facial temperatures (no BB compensation)

| Forehead | Inner canthi | Mouth | Face |
|----------|-------------|-------|------|
| TFC      | TFT         | TL    | TLmax|
| TFB      | TFR         | TFCmax| TCmax1|
| TFmax    | TFmax       | TCR   | TCmax2|
| TFE       | TCRmax      | CEmax | Tmax  |
| T̅C       | T̅CLmax      |
| T̅CR      | T̅CRmax      |
| T̅C_max   | T̅Cmax1      |

IRT-1: 0.79 0.78 0.80 0.77 0.80 0.83 0.87 0.85 0.87 0.87 0.91 0.89 0.91 0.88 0.92
IRT-2: 0.81 0.79 0.81 0.78 0.78 0.84 0.87 0.89 0.85 0.88 0.90 0.93 0.93 0.86 0.94

4. Discussion

In an extensive clinical study, we have evaluated the use of IRTs under standardized conditions and collected a wide range of data on facial temperatures and their correlation to oral measurements. These data have yielded valuable insights into IRT-based temperature estimation and fever detection capabilities and the factors that impact system performance.

4.1 Thermographic screening accuracy and standardization

This study was largely based on two international consensus documents described above – IEC 80601-2-59 and ISO/TR 13154\textsuperscript{23,24}. The guidance provided by these publications helped ensure that the devices used in this research had a high level of image quality and that the acquisition methods – including instructions to subjects – were optimized to enable accurate measurements. The optimal approaches identified in our study produced results that were equal to or better than most prior relevant works in terms of absolute agreement with, and correlation to, reference measurements, as well as discrimination of febrile subjects.

Our findings showed that the differences between $T_{\text{ref}}$ and temperatures of different facial regions were in the ranges of 1.6-2.8 °C for the forehead region, 1.4-2.4 °C for the inner canthi regions, 1.7-1.8 °C for the mouth region and 1.2-1.3 °C for the maximum face temperature. The magnitude of these results is smaller than results from Nguyen et al. who showed differences in the range of 2.1-8.7 °C between $T_{\text{ref}}$ and facial maximum temperature by three IRTs\textsuperscript{17}; similarly Chan et al. showed forehead temperatures differences of 3.0 °C and 3.9 °C for febrile and non-febrile subjects, respectively\textsuperscript{18}. Our results also showed strong correlations between IRT-measured temperatures ($T_{\text{IRT}}$) and $T_{\text{ref}}$, with both IRTs producing $r$ values as high as the 0.75-0.80 range. These values are much higher than several prior studies that found $r$ values between IRT and oral temperatures of no greater than 0.45\textsuperscript{2,17,39}. Scatter plots of $T_{\text{IRT}}$ vs. $T_{\text{ref}}$ provided in prior studies, such as Chan et al.\textsuperscript{18}, also do not show the strong linear trends seen in our $T_{\text{max}}$ and $T_{T\text{Emax}}$ data (Figure 5). It is likely that this improvement in correlation is due to control methods that help to reduce measurement variability, including stability correction with a blackbody, reduction of confounding environmental factors, multi-frame averaging, and the use of canthi regions in thermal images.

Strong temperature correlations enabled discrimination between febrile and afebrile subjects to a high degree of accuracy. For a low-grade fever diagnostic threshold of 37.5 °C, $T_{\text{max}}$ data produced an AUC values of 0.95-0.97 and Se/Sp values in the 0.85-0.95 range. For a diagnostic threshold of 37.8 °C, Se/Sp values increased to 0.93-0.95. These results for relatively low-grade fever detection, as well as findings at higher diagnostic thresholds shown in Table 5, compare favorably with the literature. In a study of airport
travelers, Priest et al. found an AUC of 0.71 (Se/Sp = 0.86/0.71) for a fever threshold of 37.5 °C using full-face maximum temperatures\textsuperscript{20}. Nishiura et al. estimated that the AUC values were 0.79 and 0.75 for threshold temperatures of 37.5°C and 38.0 °C\textsuperscript{2}. Nguyen et al. compared IRT performance for fever screening using images of the face and neck, with 37.8 °C as the fever threshold\textsuperscript{17}. In this study, AUC values of 0.96 and 0.92 were found for two IRTs, yet the corresponding $r$ values of 0.43 and 0.42 do not appear sufficient for high accuracy measurements. Hewlett et al. obtained AUC values of 0.86 and 0.90 for fever thresholds of 37.8°C and 38°C, but did not report $r$ values or results for 37.5 °C\textsuperscript{19}. These comparisons provide substantial evidence that an approach based largely on adherence to recently published standards has the potential to advance IRT-based fever screening capability.

4.2 Comparison of facial temperatures

The 17 facial temperatures extracted from each subject’s thermal image can be categorized by facial region (forehead, canthi, mouth, entire face) or by measurement location selection method (fixed-location vs. maximum value of a defined region). Analyzing our extensive clinical testing results provided insight into key trends and potential approaches for optimizing IRT-based fever screening.

IRT system performance was highly dependent on measurement location, with the forehead producing lower accuracy than canthi regions. Temperatures determined from five fixed locations on the forehead ($T_{FC}, T_{FT}, T_{FB}, T_{FL}$ and $T_{FR}$) had relatively low correlations ($r<0.50$) with $T_{ref}$ and larger pairwise differences. Fixed locations in the canthi region showed moderately strong correlations ($r$ values of 0.51 to 0.63) with $T_{ref}$ and their pairwise differences from $T_{ref}$ were also relatively small. Similarly, the maximum-value data for canthi regions showed better performance than the forehead or mouth regions. This result aligns with a prior comparison of IRT-based eye and forehead measurements\textsuperscript{43}. In our study, maximum-value of the entire face ($T_{max}$) provided better performance than the forehead ($T_{FEmax}$) in terms of correlation and fever detection; this finding is consistent with a prior study that compared maximum temperatures from the full face and forehead ($r$ values of 0.43 and 0.36, respectively)\textsuperscript{18}. Differences in performance between the forehead and inner canthi are likely due to perfusion of the canthi from the internal carotid (ophthalmic) artery, proximity to large vessels and relatively thin skin\textsuperscript{32}, whereas the forehead is more diffusely perfused and susceptible to convective and evaporative cooling\textsuperscript{43,44}. These findings may shed light on the poor sensitivity values found in some NCIT studies\textsuperscript{14}.

Overall, the maximum value in a region showed better diagnostic performance and correlation with $T_{ref}$ than the value at a fixed location within this region, with greatest $r$ values and AUC values for $T_{max}$, followed by $T_{CEmax}$ and then $T_{FEmax}$. Prior studies have also found that maximum-values approaches tended to provide greater performance\textsuperscript{18}. $T_{CEmax}$ and $T_{max}$ yielded similar $r$ values and statistically equivalent AUC values, as well as significantly higher AUC values than $T_{FEmax}$. Interestingly, Figure 5 shows that unlike the relatively tight cluster of normal-range data points ($T_{ref} = 36.4-37.4$ °C), data for $T_{Cmax1}$ exhibits a tail extending to lower IRT-measured values than other datasets. This feature is also present in the few scatter plots that have been published from clinical IRT data\textsuperscript{18,43}. Additionally, we found
that individual hairs on the forehead degraded accuracy. The improved performance observed for maximum region temperatures may be due in part to subject-to-subject variations in facial anatomy and physiology that cause unpredictable nonuniformity in spatial temperature distribution. Taking the maximum temperature of a region affords greater robustness to such variations.

As noted above, approaches involving the inner canthi or maximum-temperature locations provided higher levels of performance. Therefore, it is not surprising that $T_{CEmax}$ – which involves both of these features – provided one of the best options of the 17 temperatures tested. The finding that $T_{max}$ provided slightly better performance than $T_{CEmax}$ is a more unexpected result, because it was not advocated in IEC TR 13154 as a “robust measurement site”, as the inner canthi were. However, this approach has been used in a number of prior studies\textsuperscript{17,18,20} likely due to its combination of simplicity and effectiveness. These prior studies achieved relatively high Se/Sp values (0.7-0.9) using this approach. In part, this effectiveness stems from the fact that the inner canthi are a key thermal feature in full face images, as discussed in the following section. In spite of these benefits, there may be unresolved challenges related to the use of $T_{max}$, such as confounding physiological factors like sinusitis that impact temperature distributions\textsuperscript{24}.

4.3 Distribution of thermal maxima in full face images

In order to better understand the results obtained with $T_{max}$, we evaluated the distribution of locations where maximum temperatures occurred over 3252 thermal images collected by the two IRTs from the first round of measurements. The locations of thermal maxima in full facial images are summarized in Figure 7 and Table 10. According to Table 10, thermal maxima most commonly appeared (59.5%) in the inner canthi region, followed by oral (21.7%), forehead (8.8%), nasal (4.1%) and temporal (3.6%) regions. The predominance of inner canthi maxima is expected given what is known regarding perfusion in this region. A relatively large fraction of maxima occurred in the oral region, likely due to perfusion from the facial artery which is closer to the external carotid artery than the vessels that perfuse most facial regions. The forehead maximum were typically along the hairline, likely due to the thermal insulation effect of hair. Some thermal maxima appeared in the temporal region, likely due to the superficial temporal arteries. It was unexpected to find maxima in the nasal/nostril region (bottom); whether these are due to some pathology such as sinusitis\textsuperscript{24,45} or perhaps exhalation of warm air is not currently known.

| Region                | Number | %  |
|-----------------------|--------|----|
| Inner canthi          | 645    | 59.5|
| Oral (closed)         | 235    | 21.7|
| Forehead (hairline)   | 95     | 8.8 |
| Nasal                 | 44     | 4.1 |
| Temporal              | 39     | 3.6 |
| Neck                  | 17     | 1.6 |
| Other                 | 9      | 0.8 |

4.4 Quality of a thermographic screening system
The IEC 80601-2-59 standard defines a screening thermograph (ST) as a system composed of an IRT and an external temperature reference source (usually a blackbody with known temperature and emissivity), and in some cases, a computer and software for data acquisition, processing and storage. Therefore, most results in this paper, except for the data in Section 3.4, are technically not results of two thermal cameras, IRT-1 and IRT-2, rather, two fever screening systems, (IRT-1 + BB) and (IRT-2 + BB). We have evaluated these two systems in our previous work and found that their uniformity, stability, drift, minimum resolvable temperature difference, and laboratory accuracy all satisfied the standard requirements.

The use of a blackbody for temperature compensation had a moderate impact on IRT screening ability. In our prior study, such compensation vastly improved the stability of IRT-2, and enabled the system to meet IEC 80601-2-59 performance specifications. Except to measure and compensate for long-term drift, the use of 3-frame averaging in the current study may have improved stability to the point where the blackbody was no longer critical. If no frame averaging is used, the use of a blackbody would likely be more critical for fever detection. Additionally, the current study was executed in an environment with relatively stable ambient temperature; it is likely that in a less controlled screening location with larger, more rapid thermal fluctuations, blackbody compensation would be more important.

While inherent IRT instrumentation quality is critical, performance also depends on effective implementation. The use of control methods such as an absorbing background, multiple frame imaging, and thermally stable, forward-facing subjects. Given that many of these confounding factors have been addressed in our study, the results presented here likely indicate a best-case performance level. As control methods we have implemented are removed – which may be necessary in certain real-world screening situations – it is likely that performance will degrade. The degree to which removal of any specific control will impact results is beyond the scope of the current study but may be important for predicting real-world performance.

4.5 Fever screening during an epidemic

The primary purpose of this study was to facilitate the implementation of IRT systems and practices that enable optimal measurement accuracy and highly effective fever screening during epidemics. However, achieving effective screening can be a complex process, as many factors need to be addressed beyond the physics, instrumentation and acquisition procedures. While our results showed that some facial temperatures had good discrimination abilities with high AUC values, some previous literature claimed that thermography was not highly effective for fever screening during disease outbreaks. This may have been due to device instability, inappropriate temperature reading locations, nonstandard calibration and environmental controls.

The frequency at which fever presents as a symptom is another impediment to successful screening. In the current COVID-19 outbreak, many of those infected are largely asymptomatic and only 73% have exhibited a fever; in 2009, only half of H1N1 outbreak cases had temperatures of ≥37.8 °C; and a 2011 study indicated that none of the 30 subjects identified as being flu-infected had a temperature of 37.8 °C or greater, and only two had a temperature of 37.5 °C. Therefore, while IRT-based screening can detect
individuals with elevated temperature, it is not a viable stand-alone tool for screening for individuals infected with specific diseases\textsuperscript{49}. It may play an adjunct role along with other screening evaluations. Since fever is only one common symptom of infectious disease, an effective screening process should include evaluation of a range of symptoms\textsuperscript{3,7,8}. The future development of an integrative screening system may include thermography along with optical imaging approaches for evaluation of vital signs such as heart and respiration rate as well as other physiological parameters\textsuperscript{8}.

Given that $T_{C E m a x}$ and $T_{m a x}$ provided the best performance, it is worth considering issues that might influence the decision to implement one approach or the other. Acquiring a full-face region for calculation of $T_{m a x}$ would likely be easier to accomplish and performed more reliably than determining $T_{C E m a x}$ via auxiliary visible light imaging and computationally-intensive techniques for co-registration of inner canthi regions. This may be particularly important in a high throughput situation where delays due to computer processing or image co-registration errors could become highly inconvenient. However, implementing an approach that blindly determines the maximum temperature from a full-face thermal image may increase the need to identify confounding pathological/physiological conditions such as sinusitis\textsuperscript{24,45,50}. To accomplish this task rapidly and effectively may require significant screener training, although automated approaches (e.g., deep learning algorithms) could also be developed to augment or replace manual assessments.

Another practical challenge involves the identification of an appropriate reference temperature diagnostic threshold, given the diversity of values that have been implemented. The Centers for Disease Control and Prevention (CDC) has recommended the use of 38°C\textsuperscript{51}, whereas prior human subject studies have been based on 37.5 °C\textsuperscript{7,39,40}, 37.6 °C\textsuperscript{52}, 37.7 °C\textsuperscript{32,48}, 37.8 °C\textsuperscript{17,19,20}, and 38 °C\textsuperscript{35}. Different thresholds have been used for different outbreaks, such as ≥ 38°C for SARS \textsuperscript{1} and 37.7°C for adults and 37.9 °C for children in an H1N1 study\textsuperscript{8}. The literature indicates that as the threshold temperature decreases, diagnostic accuracy typically degrades. Uncertainty in normal body temperatures – which can be influenced by gender, age, physical exertion and other factors – can further increase error in screening tasks\textsuperscript{15,35,39,53}. Additionally, a recent study indicates that normal body temperature has decreased on average since the establishment of the 37 °C threshold 150 years ago\textsuperscript{54}. In spite of these obstacles, our results indicated that IRT systems are capable of detecting low-grade fever (37.5 °C) in subjects, which could mean that early-stage infections and those producing only moderate symptoms could be more readily identified. The significance of this ability is demonstrated by the fact that of the subjects with $T_{r e f}$ values over 37.5 °C in our study, 60% would not have exceeded the CDC recommended diagnostic threshold of 38 °C.

Even if a suitable diagnostic threshold for fever based on body temperature can be defined, determining the IRT cut-off temperature for fever screening requires a variety of considerations. While we calculated optimal cut-off temperature to optimize both Se and Sp, this may not represent an optimal value for real-world use. For a severe disease, lower cut-off values may be needed to minimize false negatives in primary screening. Given the typically low prevalence of diseased individuals in a screening population, the false positive rate in primary screening will be high (and thus the positive predictive value low). On the other hand, it may also
be important to balance the burden on the population being screened (e.g., travel delays) and screening personnel (e.g., workload, fatigue, cost to health agencies)\textsuperscript{17,39}.

5. Conclusions

Overall, our clinical study results support the conclusion that adherence to international consensus guidelines regarding IRT system specifications and implementation contributes to optimization of measurement accuracy and detection of febrile individuals. These guidelines include environmental controls as well as subject preparations and acclimation prior to measurements. Two additional findings were made: first, targeted measurement of a small inner canthi area may be unnecessary, with full face maximum temperatures providing the best performance followed closely by the maximum of a wider inner canthi region. Second, while temperature compensation with a high-quality blackbody can improve IRT system performance, the impact was modest on our highly controlled setup, which incorporated multi-frame averaging. Our findings also indicated that forehead temperatures provide generally inferior estimation of oral temperature relative to the inner canthi. The optimal approaches identified here achieved correlation coefficients of \( \sim 0.75 \), as well as AUC values of \( \sim 0.95 \) for detection of low-grade (37.5 °C) fever. This capacity may facilitate detection of a wider range of disease presentations than a less accurate method would allow. Future work will involve further analysis of our clinical study results to address the impact of confounding factors relating to inter-subject and environmental variability.

Declarations

Acknowledgments

This research was funded by the U.S. Food and Drug Administration’s Medical Countermeasures Initiative (MCMi) Regulatory Science Program (Fund# 16ECDRH407). The authors gratefully acknowledge Dr. Stacey Sullivan, who evaluated the oral thermometer and prepared the operation manual; Ms. Jean Rinaldi, who helped to prepare the clinical study protocol and recruitment documents; the University Health Center of the University of Maryland at College Park for their outstanding collaboration with the research team; Peter Tan, Monica Chu, Peter Chin, Pooneh Azadikhah, Oluwatobi Fagbohun, Shira Winston, Jacqueline Dempsey, Muzammil Quadir, Madison Varvaris and Raqel Pryor for their assistance with data collection; and Drs. Zane Arp, Daniel X. Hammer, William C. Vogt and Jessica Lamb for editorial contributions to this manuscript.

Author Contributions

Q.W., T.J.P. and J.C. conceptualized the project. Q.W. obtained IRB approval and led the whole project. D.M. provided advices and space for the clinical study. P.G. led the clinical data collection. Y.Z. analyzed the data, with the help from M.C. Y.Z., Q.W, and T.J.P. wrote the initial draft of this manuscript. All authors edited and reviewed the manuscript.

Disclaimer
The mention of commercial products, their sources, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products by the Department of Health and Human Services. This paper only represents the authors’ opinion, not FDA recommendations/policy. The authors declare that they have no competing interests.

References

1. Chiu, W. et al. Infrared thermography to mass-screen suspected SARS patients with fever. Asia-Pac. J. Public Health 17, 26-28 (2005).

2. Nishiura, H. & Kamiya, K. Fever screening during the influenza (H1N1-2009) pandemic at Narita International Airport, Japan. BMC Infect. Dis. 11, 111 (2011).

3. Shi, H. et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect. Dis. (2020).

4. Yang, X. et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir. Med. (2020).

5. Goeijenbier, M., Van Kampen, J., Reusken, C., Koopmans, M. & Van Gorp, E. Ebola virus disease: a review on epidemiology, symptoms, treatment and pathogenesis. J. Med. 72, 442-448 (2014).

6. Huang, C. et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet 395, 497-506 (2020).

7. Liu, C.-C., Chang, R.-E. & Chang, W.-C. Limitations of forehead infrared body temperature detection for fever screening for severe acute respiratory syndrome. Control Hosp. Epidemiol. 25, 1109-1111 (2004).

8. Ng, E. Y. K. Thermal imager as fever identification tool for infectious diseases outbreak. in Medical Infrared Imaging: Principles and Practices (eds Mary Diakides, Joseph D. Bronzino, & Donald R. Peterson) Ch. 24, 1–19 (CRC Press, 2013).

9. Chiappini, E. et al. Performance of non-contact infrared thermometer for detecting febrile children in hospital and ambulatory settings. Clin. Nursing 20, 1311-1318 (2011).

10. Teran, C. et al. Clinical accuracy of a non-contact infrared skin thermometer in paediatric practice. Child Care Health Dev. 38, 471-476 (2011).

11. Ng, E. Y. K. & Acharya, R. U. Remote-sensing infrared thermography. IEEE Eng. Med. Biol. Mag. 28, 76-83 (2009).

12. Usamentiaga, R. et al. Infrared thermography for temperature measurement and non-destructive testing. Sensors 14, 12305-12348 (2014).

13. American Society for Testing and Materials. ASTM E1965-98: Standard Specification for Infrared Thermometers for Intermittent Determination of Patient Temperature. (2016).

14. Bitar, D., Goubar, A. & Desenclos, J. International travels and fever screening during epidemics: a literature review on the effectiveness and potential use of non-contact infrared thermometers. Euro Surveill. 14, 19115 (2009).
15. Selent, M. U. *et al.* Mass screening for fever in children: a comparison of 3 infrared thermal detection.*Pediatr. Emerg. Care* **29**, 305-313 (2013).

16. Tay, Y., Low, Y., Zhao, X., Cook, A. & Lee, V. Comparison of Infrared Thermal Detection Systems for mass screening in a tropical healthcare setting. *Public Health* **129**, 1471-1478 (2015).

17. Nguyen, A. V. *et al.* Comparison of 3 infrared thermal detection systems and self-report for mass fever *Emerging Infect. Dis.* **16**, 1710-1717 (2010).

18. Chan, L. L., Kumana, C. R. & Cheung, B. M. Utility of infrared thermography for screening febrile subjects. *Hong Kong Med. J.* **19**, 109-115 (2013).

19. Hewlett, A. L., Kalil, A. C., Strum, R. A., Zeger, W. G. & Smith, P. W. Evaluation of an infrared thermal detection system for fever recognition during the H1N1 influenza pandemic. *Control Hosp. Epidemiol.* **32**, 504-506 (2011).

20. Priest, C., Duncan, A. R., Jennings, L. C. & Baker, M. G. Thermal Image Scanning for Influenza Border Screening: Results of an Airport Screening Study. *PLoS One* **6**, e14490 (2011).

21. Cho, K. S. & Yoon, J. Fever screening and detection of febrile arrivals at an international airport in Korea: association among self-reported fever, infrared thermal camera scanning, and tympanic temperature. *Health* **36**, 4 (2014).

22. Mouchtouri, V. A. *et al.* Exit and entry screening practices for infectious diseases among travelers at points of entry: looking for evidence on public health impact. *J. Env. Res. Public Health* **16**, 4638 (2019).

23. International Electrotechnical Commission & International Organization for Standardization. IEC 80601-2-59: Medical electrical equipment - Part 2-59: Particular requirements for the basic safety and essential performance of screening thermographs for human febrile temperature screening. (2017).

24. International Organization for Standardization. ISO/TR 13154: Medical electrical equipment — Deployment, implementation and operational guidelines for identifying febrile humans using a screening thermograph. (2017).

25. Holshue, M. L. *et al.* First case of 2019 novel coronavirus in the United States. *New Engl. J. Med.* (2020).

26. Woelfel, *et al.* Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster. *medRxiv* (2020).

27. Geneva, I. I., Cuzzo, B., Fazili, T. & Javaid, W. Normal body temperature: a systematic review. *Open Forum Infect. Dis.* **6**, ofz032 (2019).

28. Ghassemi, P., Pfefer, T. J., Casamento, J. P., Simpson, R. & Wang, Q. Best practices for standardized performance testing of infrared thermographs intended for fever screening. *PLoS One* **13**, e0203302 (2018).

29. Mairiaux, P., Sagot, J. & Candas, V. Oral temperature as an index of core temperature during heat *Eur. J. Appl. Physiol. Occup. Physiol.* **50**, 331-341 (1983).

30. Ng, D. K., Chan, C.-H., Chow, P-Y. & Kwok, K.-L. Infrared ear thermometry. *J. Gen. Pract.* **54**, 869-869 (2004).
31. Mercer, J. B. & Ring, E. F. J. Fever screening and infrared thermal imaging: concerns and guidelines. *Int. 19*, 67-69 (2009).
32. Ng, E. Y. K., Muljo, W. & Wong, B. S. Study of facial skin and aural temperature. *IEEE Eng. Med. Biol. 25*, 68-74 (2006).
33. Sun, , Matsui, T., Kirimoto, T., Yao, Y. & Abe, S. Applications of infrared thermography for noncontact and noninvasive mass screening of febrile international travelers at airport quarantine stations. in *Application of Infrared to Biomedical Sciences* (eds E.Y.K. Ng & M. Etehadtavakol) 347-358 (Springer, 2017).
34. Chan, L. S., Cheung, G. T., Lauder, I. J. & Kumana, C. R. Screening for fever by remote-sensing infrared thermographic camera. *Travel Med. 11*, 273-279 (2004).
35. Ng, D. K., Chan, C. H., Lee, R. S. & Leung, L. C. Non-contact infrared thermometry temperature measurement for screening fever in children. *Trop. Paediatr. 25*, 267-275 (2005).
36. Steketee, J. Spectral emissivity of skin and pericardium. *Med. Biol. 18*, 686 (1973).
37. Chenna, Y. N. D., Ghassemi, P., Pfefer, T. J., Casamento, J. & Wang, Q. Free-form deformation approach for registration of visible and infrared facial images in fever screening. *Sensors 18*, 125 (2018).
38. Kumar, R. & Indrayan, A. Receiver operating characteristic (ROC) curve for medical researchers. *Indian 48*, 277-287 (2011).
39. Cheung, B., Chan, L., Lauder, I. & Kumana, C. Detection of body temperature with infrared thermography: accuracy in detection of fever. *Hong Kong Med. J. 18*, 31-34 (2012).
40. World Health WHO informal consultation on fever management in peripheral health care settings: a global review of evidence and practice. (2013).
41. Youden, W. J. Index for rating diagnostic tests. *Cancer 3*, 32-35 (1950).
42. Mendt, S. *et al.* Circadian rhythms in bed rest: monitoring core body temperature via heat-flux approach is superior to skin surface temperature. *Int. 34*, 666-676 (2017).
43. Ng, E. Y. K., Kaw, G. J. L. & Chang, W. M. Analysis of IR thermal imager for mass blind fever *Microvasc. Res. 68*, 104-109 (2004).
44. Ring, F. J. & Ng, E. Y. K. Infrared thermal imaging standards for human fever detection. in *Medical infrared imaging: principles and practices* (eds Mary Diakides, Joseph D Bronzino, & Donald R Peterson) Ch. 22, 1-5 (CRC press, 2012).
45. Mansfield, C. D., Attas, E. M. & Gall, R. M. Evaluation of static thermal and near-infrared hyperspectral imaging for the diagnosis of acute maxillary rhinosinusitis. *Otolaryngol. 34*, 99-108 (2005).
46. Perkins, M. D. & Kessel, M. What Ebola tells us about outbreak diagnostic readiness. *Biotechnol. 33*, 464 (2015).
47. Mabey, D., Flasche, S. & Edmunds, W. J. Airport screening for Ebola. *The BMJ 349*, g6202 (2014).
48. Ng, E. Y. K. Is thermal scanner losing its bite in mass screening of fever due to SARS? *Phys. 32*, 93-97 (2005).
49. Quilty, B. J. & Clifford, S. Effectiveness of airport screening at detecting travellers infected with novel coronavirus (2019-nCoV). *Euro Surveill.* 25 (2020).

50. Niedzielska,, Pawelec, S. & Puszczewicz, Z. The employment of thermographic examinations in the diagnostics of diseases of the paranasal sinuses. *Dentomaxillofac. Radiol.* 46, 20160367 (2017).

51. Center for Disease Control and Prevention. COVID-19_CAREKit: Check and record everyday. (2020).

52. Ring, F. J. *et al.* Infrared thermal imaging for fever detection in children. in *Medical Infrared Imaging: Principles and Practices* (eds Mary Diakides, Joseph D. Bronzino, & Donald R. Peterson) Ch. 23, 1-5 (CRC Press, 2013).

53. Mackowiak, P. A. Concepts of fever. *Intern. Med.* 158, 1870-1881 (1998).

54. Protsiv, M., Ley, C., Lankester, J., Hastie, T. & Parsonnet, J. Decreasing human body temperature in the United States since the Industrial Revolution. *eLife* 9, e49555 (2020).

**Figures**

**Figure 1**

Setup of the screening room
Figure 2

Flowchart of temperature measurement procedure – only data from the steps labeled in green were used in this study.

Figure 3

Delineated facial regions and critical points on (a) visible light and (b) thermal images: forehead regions and points (green), canthi region and points (red), mouth region (gray rectangle) and entire face (blue rectangle).
Figure 4

Boxplots of pairwise differences between IRT-measured facial temperatures and $T_{ref}$. Note that $T_{IRT}$ on the y axis represents all the IRT-measured facial temperatures on the x axis.
Figure 5

Scatter plots of TCmax1, TFEmax, TCEmax and Tmax versus Tref, with linear fits and correlation coefficients.

Figure 6

ROC curves for febrile subject (Tref ≥ 37.5 °C) detection with (a) IRT-1 and (b) IRT-2 using imaging temperatures of Tmax, TCEmax, TCmax1 and TFEmax.
Figure 7

IRT images illustrating (a) delineation of regions for thermal maxima analysis and (b-i) examples of maxima in human subjects. Photos are of author Q. Wang.