2011

Efficacy of Fixed Infrared Thermography for Identification of Subjects with Influenza-like Illness

Christopher M. Hinnerichs

Walden University

COLLEGE OF HEALTH SCIENCES

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Christopher M. Hinnerichs

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Dr. Angela Prehn, Committee Chairperson, Public Health Faculty
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Chief Academic Officer

David Clinefelter, Ph.D.

Walden University

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MS, University of New Mexico, 2006

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Doctor of Philosophy

Public Health, Epidemiology

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Abstract

Due to pandemic threats and the occurrence of biological terrorism, technological advancements are being vetted, developed, and implemented as part of surveillance systems and tools. A potential surveillance tool is infrared thermography (IRT), and its efficacy for screening was the focus of this dissertation. IRT-screened participants' temperatures were compared to laboratory diagnostics to confirm the presence or absence of influenza-like illness (ILI). An archival dataset of personnel on United States Navy and Marine vessels that were identified as exceeding an ILI threshold limit provided the data for the 320 study participants. Using a guiding thermo-science framework, derived from past IRT studies, the primary research question concerned whether IRT could statistically differentiate between afebrile participants (without ILI) and febrile participants (with ILI) using receiver operating characteristics (ROC). Results showed that IRT could differentiate between febrile and afebrile participants 91% of the time (ROC = 0.91; $\chi^2 = 230.71$, $p = < 0.01$), indicating excellent efficacy in this study setting. In addition, the correlation between oral temperatures and IRT surface temperatures was analyzed by gender. A strong correlation between the two variables for males ($r = 0.90$, n = 226, $p < 0.01$) and females ($r = 0.87$, n = 94, $p < 0.01$) was shown with little variance between the genders (*observed z* = 1.12, *SE* = 0.26). These findings have significant positive social change implications as they could provide senior public health decision makers with informed knowledge of IRTs benefits and limitations for rapid screening of febrile individuals in public settings to impede the transmission of ILI.

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ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 - 1346

Dedication

I would like to dedicate this dissertation to my family and friends. These amazing individuals have truly been my support throughout these challenging times, celebrated in my victories, and always encouraged me during shortfalls along this academic process. Their prayers, guidance, and motivation instilled and sustained the strength in me to push for this dream to come into fruition.

Acknowledgements

I am truly grateful to my committee chair, Dr. Angela Prehn, for her judicious responses, eye for detail, and encouragement and for asking the hard questions that strengthened my dissertation and learning process. To my board member Dr. German Gonzalez, I greatly appreciated your clinical insight, depth, and knowledge that bolstered my research while providing me with a reality check when the content ventured outside my epidemiologic lane of proficiency. To my colleague and friend, Dr. Jesse Monestersky, who provided additional clinical and oversight support, linkage to my research population, mentorship, and encouragement along this road – thank you tremendously. In addition, I would like to thank Brenda Crabtree for being my microbiology and laboratory subject matter expert – her explanations of the diagnostic results and recommendations were invaluable. To the Pacific Command Surgeon's Office, thank you for the dedicated time that allowed me to center on my research, encouragement along the way, and exemplar leadership that I will emulate throughout my career. I would like to acknowledge my parents, Dr. Terry and Cheryle Hinnerichs, for their astute guidance, support, and their own personal achievements that motivated me to never relinquish what I started. To my brother, Todd Hinnerichs, for his humor, inspiration, and successful career path that further inspired me to push the limits and not settle for mediocrity.

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Chapter 1: Introduction to the Study

Introduction

Globally, public health has experienced the burden of endemic, epidemic, and pandemic infectious diseases. Outbreaks of highly pathogenic avian influenza (H5N1), severe acute respiratory syndrome (SARS), and the 2009 H1N1 pandemic influenza are recent examples that have challenged public health resources (Centers for Disease Control and Prevention [CDC], 2010f). Although the virulence of these pathogens has varied considerably, in sum they have contributed to thousands of lives lost and strained the response capacity of public health and health care systems. These outbreaks have also exposed waning community resilience (i.e., ability to quickly recover and resume normal duties) at peak incidence periods (Powdrill, Nipp, & Rinderknecht, 2010). During these crises, government public health planning, human resource allocation, and international communication and reporting of infectious diseases ceased to exist in adequate quantities to properly guard the public's health (United States Department of Health and Human Services [USDHHS], 2009).

Community resilience is predicated upon a strong and sustainable public health network, robust healthcare systems, and sufficient emergency response capabilities. This matter requires the healthcare infrastructure to be capable of meeting anticipated biological threats (e.g., influenza-like illnesses [ILI]) and to have the capability to react effectively in the event of unanticipated threats. Resilience may be achieved by a vigilant state of readiness, capacity to prevent and mitigate nascent infectious diseases, forewarning to alert public health officials when baseline infectious disease thresholds have been exceeded, and the ability to mobilize responders and equipment in a timely

manner (CDC, 2010f). Thus, anticipation, vigilance, and readiness are essential functions of surveillance—the first line of defense against emerging infectious diseases (USDHHS, 2009).

In the United States, at points of debarkation and embarkation there are limited passive surveillance means to screen travelers who might harbor infectious diseases as they enter U.S. borders (Evans & Thibeault, 2009). These vulnerable entry points rely on self-report health status surveys from travelers and reports of evident ailing travelers from aviation crew members (John, King, & Jong, 2005). To compound this issue, each year approximately 50 million people travel from industrialized nations to developing nations, yet only 8 to 19% of ill travelers consulted a physician after returning home (Winter & Alkan, 2002). As a result, the true etiology of their illness remains unknown (Hill, 2000). Most importantly, infectious diseases do not respect geographic borders, and public health officials at vulnerable points of embarkation and debarkation (viz., airports, seaports, and rail and bus stations) must enhance procedures to identify and provide immediate care to infectious individuals as well as to impede further spread of disease using passive and quantifiable forms of surveillance.

Surveillance in the public health domain is the continuous, collaborative aggregation, analysis, understanding, frequency, and distribution of health-related data in efforts to reduce community morbidity and mortality; it is the quintessential tool for supporting the labors of public health's functions (CDC, 2004). More specifically, it provides the baseline information that aids public health interventions, provides means to evaluate the burden of disease within communities, allows researchers to understand the natural history of disease within a region, fosters and germinates thought for future

research, and facilitates planning efforts. Most importantly, public health surveillance provides a vigilant and sentinel barrier that could identify lurking biological threats.

Typically, public health surveillance has been identified through the use of reportable disease registries, healthcare providers, and laboratory reporting channels that alert public health officials about abnormal trends of communicable disease (CDC, 2007). Due to the heightened awareness of ILIs becoming pandemic threats (e.g., public attention from novel H1N1 influenza virus) and of the occurrence of biological terrorism, increasing technological advancements are being vetted, developed, and implemented as part of surveillance systems and tools (Danzig, 2008). However, these tools and systems are not stand alone devices. They must work concomitantly with all layers of surveillance, which feed into a central database for analysis and reporting to federal, state, and local officials (Powdrill, Nipp, & Rinderknecht, 2010). One of the newer disease surveillance tools is infrared thermography (IRT), and its efficacy is the focus of this dissertation.

In general, IRT is a camera system that is sensitive to infrared emittance (e.g., heat). Accordingly, various materials can be screened with this device, and their surface temperatures can be measured, including human skin (e.g., the detection of fever). Due to the device's rapid ability to acquire a surface temperature reading (~ 0.5 seconds), its noncontact with the subject being screened, and the fact that fever is a common symptom that accompanies ILIs (CDC, 2010e), IRT has been considered a viable option for public health ILI screening.

Although considerable information on IRT as a technology exists, prior research on IRT as a disease surveillance tool has been limited in scope. Studies have mainly

explored IRTs ability to function as a proxy to clinical thermometers for estimating core temperatures (Chiang et al., 2008). A few studies have examined various anatomical regions to quantify the highest surface temperature yield when using IRT, investigated the limitations of various IRT equipment and procedures for screening IRT participants, and explored environmental influences that may affect IRT measurements (Ng, Kaw, & Chang, 2004; Ng, Chan, Lee, & Leung, 2005; Ring et al., 2008). A comprehensive discussion of these studies, along with literature on ILIs, surveillance and IRT, IR impeding materials, and calibrations affecting IRT measurements will be presented in chapter 2.

Problem Statement

Researchers examining IRT and its use in mass screening of ILI have primarily investigated this technology's efficacy against aural and oral clinical thermometer readings (Chan, Cheung, Lauder, & Kumana, 2004; Cheung, Chan, Lauder, & Kumana, 2008; Chiang et al., 2008; Chiu et al., 2005; Hausfater, Zhao, Defrenne, Bonnet, & Riou, 2008; Liu, Chang, & Chang, 2004; Ng, 2005; Ng et al., 2004; Ng, Chan, Lee, & Leung, 2005; Nguyen et al., 2009a; Ring et al., 2008; Ring, McEvoy, Jung, Zuber, & Machin, 2010). Based on these studies, researchers have made the assumptive leap that elevated surface temperatures from IRT measurements serve as a predictor of ILI and that IRT can differentiate between febrile (with ILI) and afebrile (without ILI) individuals, even though a multitude of physiological responses can cause an elevated surface temperature, not necessarily indicating ILI. No known IRT research has been conducted that compares clinical diagnostics of sampled IRT participants to confirm the absence or occurrence of ILI after they have been screened; this practice could explain

whether IRT is selecting only febrile subjects with ILI or all subjects with elevated surface temperature (with or without ILI exposure). Further studies must be conducted to fully explore the efficacy of IRT for identification of ILI subjects.

Additionally, the IRT literature has shown a discrepancy between gender with regards to the accuracy of IRT surface temperature measurement (Nguyen et al., 2009; Ring et al., 2008). These differences could pose a significant impediment to this technology if IRT cannot objectively measure surface temperature equally in males and females or if adjustments for those differences cannot be made. Accordingly, gender differences in the correlations between IRT surface temperature measurements and corresponding oral temperatures were assessed.

Nature of the Study

This retrospective cross-sectional study was designed to analyze the efficacy of fixed IRT to identify subjects with ILI based on their surface temperatures. All participants screened by IRT were diagnostically compared to laboratory results from a microneutralization assay/polymerase chain reaction (PCR) to confirm the presence, absence, or exposure to disease. The analysis was accomplished using receiver operating characteristics (ROC) by studying the area under the curve (AUC) of a ROC plot that assessed the ability of IRT to differentiate between febrile (with ILI) and afebrile (without ILI) participants. ROC outputs were interpreted as (a) excellent differentiation (0.90 - 1.0), (b) good differentiation (0.80 - 0.89), (c) moderate differentiation (0.70 - 0.79), (d) poor differentiation (0.60 - 0.69), and (e) failed differentiation (0.50 - 0.59) to show efficacy of this screening tool (Hanley & McNeil, 1982; Swets, Dawes, &

Monahan, 2000). Additionally, the correlation between oral temperatures and IRT surface temperatures was analyzed by gender.

The archived data for this study came from personnel on the United States Navy and Marine vessels that were afloat in the Pacific Ocean during the 2010-2011 northern hemisphere influenza season. Eligible vessels were identified through the public health alert system (PHAS) as exceeding an ILI threshold limit within their personnel. At that time, a public health team was identified by Pacific Fleet to investigate the ship. The public health team collected blood samples, took nasopharyngeal/oropharengeal swabs, oral temperatures, IRT surface temperatures, and recorded health questionnaire data and environmental ambient conditions solely for naval outbreak investigational research. In addition, the previous data results were requested from the public health research team and used in this study to research the efficacy of fixed IRT for identification of subjects with ILI.

Research Questions and Hypotheses

1. Can IRT in a mass screening shipboard environment statistically differentiate between afebrile participants without ILI exposure and febrile participants with ILI exposure?

H_A1: In a mass screening shipboard environment, there is an association between individuals identified as febrile by IRT and individuals identified as having ILI through laboratory confirmation.

$H_0 1$: In a mass screening shipboard environment, there is no association between individuals identified as febrile by IRT and individuals identified as having ILI through laboratory confirmation.

H_A2: In a mass screening shipboard environment, there is an association between individuals identified as afebrile by IRT and individuals identified as not having ILI through laboratory confirmation.

$H_0 2$: In a mass screening shipboard environment, there is no association between individuals identified as afebrile by IRT and individuals identified as not having ILI through laboratory confirmation.

2. Does the relationship between oral and IRT surface temperatures vary by gender; in other words, does the efficacy of IRT for screening and identifying subjects with ILI differ between males and females?

H_A3: The relationship between oral and IRT surface temperatures does vary by gender.

$H_0 3$: The relationship between oral and IRT surface temperatures does not vary by gender.

Purpose of the Study

The purpose of this quantitative study was to explore the efficacy of fixed IRT for identification of subjects with ILI (viz., seasonal influenza strains) determined through IRT surface temperature differentiation between febrile (≥ 37.5°C) and afebrile (≤ 37.4°C) participants and then compared to diagnostic confirmation of disease from those participants. Additionally, the aims of this research were to further study the possible gender discrepancy in the correlation between IRT surface temperatures and oral thermometry measurements.

Conceptual Framework

The review of the IRT literature revealed particular focus on three distinct areas of research: (a) environmental influences affecting IRT measurements, (b) highest thermal yield anatomical region for IRT screening, and (c) IRT correlation to aural and oral measurements. Together, these areas provided the conceptual and guiding framework for the focus of this study (see Figure 1).

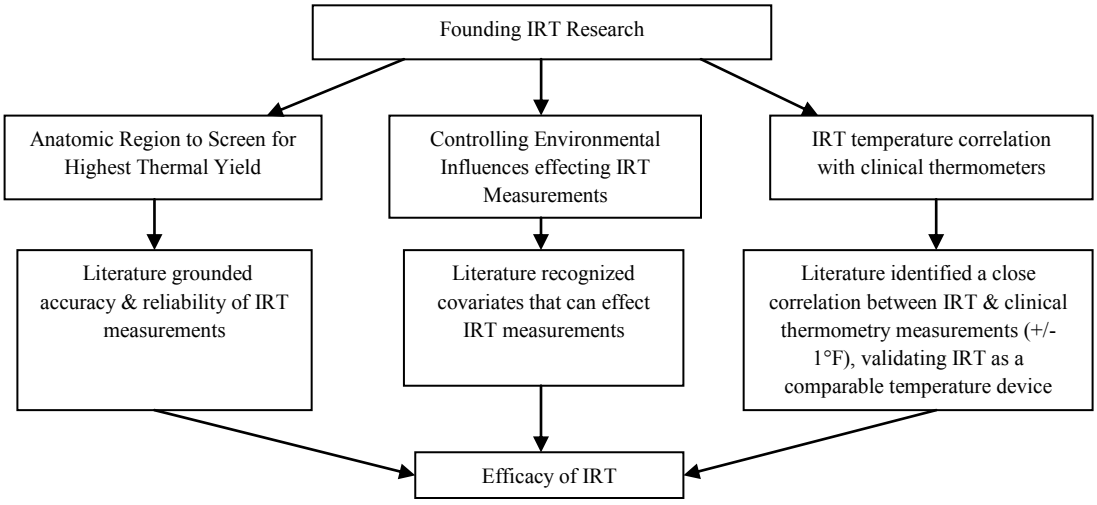

Figure 1. Illustration of IRT conceptual framework.

First, environmental influences such as humidity, excessive room temperature, and wind turbidity have been suggested to affect IRT measurements and are discussed further in chapter 2 (Chan et al., 2004; Chiang et al., 2008; Chiu et al., 2005; Ng et al., 2004; Ng et al., 2005; Nguyen et al., 2009; Ring et al., 2008). Second, Ng et al.'s (2004) research focused on the medial canthus as the region that emits the highest thermal yield and was further supported in other studies and a technical reference (viz., Chiu et al., 2005; International Standards Organization [ISO], 2008; Ng et al., 2005, Ring et al., 2008). Third, the literature demonstrated IRTs ability to function as a proxy

to clinical thermometers and to differentiate between normal temperature and elevated temperature subjects (Chan et al., 2004; Chiang et al., 2008; Liu et al., 2004; Ng et al., 2004; Ng et al., 2005; Nguyen et al., 2009; Ring et al., 2008). These three areas in the IRT literature lend to IRT efficacy – knowing that the main objectives of this technology are to parallel oral/aural thermometry readings rapidly and accurately to identify febrile subjects. Nonetheless, there appear to be no data that diagnostically confirm whether IRT is truly identifying individuals with ILI based on their surface temperatures and whether this technology can differentiate between febrile (with ILI) and afebrile (without ILI) individuals. Consequently, the three focus areas mentioned in this section provided the framework for this study to explore further the efficacy of fixed IRT for identification of subjects with ILI.

Definitions of Terms

A clear understanding of the terms and acronyms used throughout the IRT and infectious disease literature is crucial for the complete understanding and extent of this research. Accordingly, the following list will serve as the fundamental terms and acronyms used throughout this research.

Blackbody: An object that absorbs all electromagnetic radiation falling upon it and radiates this energy in a characteristic and continuous spectrum. The blackbody offers a consistent average (thermal equilibrium) of the environmental temperature being measured (Robitaille, 2004).

Calibration: Set of operations that establish, under specific parameters, the relationship between values of quantities indicated by a measuring instrument or

measuring system or values represented by a material measure or a reference material and the corresponding values realized by standards (ISO, 2008).

Calibration source: Infrared radiation (IR) blackbody reference of known and detectable temperature and emissivity (ISO, 2008).

Emissivity (ε): A ratio of the emitted thermal release of electromagnetic energy emitted by an object as a consequence of its temperature transmitted in a given direction, per unit solid angle, and per unit area projected normal in regard to that of a blackbody. Emissivity is quantified as a number between zero (typically shiny objects) and one (typically dark and dull objects) that are characteristic of various materials (Giancoli, 1998, p. 434; ISO, 2008).

Emittance: The absorbed energy (radiation) given off by an object not attributed to reflection; notably shiny surfaces emit less radiation, yet absorb little of the radiation by other objects and sources (Giancoli, 1998, p. 433).

Fixed infrared thermography: Tripod mounted IRT for maintenance of proper camera angle and consistent distance between subject and IRT during screening.

Influenza like illness (ILI): Fever (≥ 100°F) and a cough and/or an irritated throat in the absence of a known cause other than influenza (CDCh, 2010).

Infrared thermography (IRT): An apparatus that can detect infrared radiation emitted from the face in which a thermogram (image acquired from infrared emittance) is obtained from target, obtains a temperature reading from the target, and compares this reading to a set threshold temperature; IRT is also referred to as noncontact infrared thermography, infrared thermal detection system, infrared thermograph, infrared thermometry, thermal imaging, pyrometer, pyrometry, or thermal screening (ISO, 2008).

IRT efficacy: IRTs ability to distinguish between febrile and afebrile individuals ≥ 90% of the time (based on ROC analysis) and with a sensitivity ≥ 80% and specificity ≥ 75% (Hanley & McNeil, 1982; Ng, Kaw, & Chang, 2004; Swets et al., 2000).

Microneutralization assay (serum neutralization assay): A virus isolation laboratory technique for the detection of virus; assay detects the presence of neutralizing antibodies to a specific virus, which indicates exposure to that specific virus (Flint, Enquist, Racaniello, & Skalka, 2004, p. 579; Murphy, Gibbs, Horzinek, & Studdert, 1999, p. 217).

Polymerase chain reaction (PCR): Laboratory technique used to analyze DNA transcribed from the RNA virus (influenza) by using fluorescent probes to identify specific regions of the DNA specific to the influenza virus of question (Dorak, 2006, p. 12; Webster's New World Dictionary [WNWMD], 2004b).

Reflectance or reflectivity: The percentage of the total radiation falling on a body that is directly reflected, notably a blackbody reflectance is zero (Giancoli, 1998).

Seroconversion: The development of detectable antibodies in the blood as a result to an infectious agent (WNWMD, 2004c).

Skin (surface) temperature: A measurement from the workable target plane of an IRT with proper adjustments for skin emissivity (ISO, 2008).

Target: Region of the face selected for highest thermal yield (ISO, 2008).

Target plane: In-focus plane perpendicular to the line of sight of an IRT (ISO, 2008).

Workable target plane: The region of the target plane that meets specified performance IRT requirements (ISO, 2008).

Assumptions and Limitations

This study was limited to the archived data of Navy and Marine forces that were afloat within the Pacific region during the 2010-2011 northern hemisphere influenza season. Although other ships with elevated ILI crew members may have docked at Pearl Harbor, Hawaii, during the time of this study, the ship with the largest crew, medical supportive staff, and onboard PCR capabilities was selected by the public health team, as their data collection methods required diagnostic confirmation from the ship's medical staff that the cause of the outbreak was indeed ILI related.

This study had limitations that needed to be considered and interpreted in the final conclusions. For example, the participants for this study were derived from military individuals who may not completely represent the general population. All IRT participants may have not been screened for exactly 5 seconds. Another limit of this study was that participants were not screened for any preexisting medical conditions that could result in hyper or hypothermia, as medical records or self-reports for these conditions were not ascertained.

Significance of the Study

Influenza is responsible for approximately 200,000 hospitalizations per year and roughly 36,000 deaths per year in the United States alone (CDC, 2010a). The global influenza mortality rate is estimated between 250,000 to 500,000 cases per year with an approximate morbidity rate between 3 and 5 million cases per year (World Health Organization [WHO], 2010). Additionally, an estimate of the United States financial burden on hospitals due to deferment of elective admissions, uncompensated care, and uninsured patients could result in losses of $3.9 billion, or approximately $784,592 per

hospital during an influenza pandemic (Matheny, Toner, & Waldhorn, 2007). Because of the burdens influenza and ILIs can place on society, strategies are needed for rapid identification of ill individuals. Individuals infected with ILIs frequently have the common symptoms of fever, cough, and sore throat (CDC, 2010e). IRT could be a primary sentinel tool for public health officials to screen and identify febrile individuals at mass gathering points (e.g., schools, office buildings, hospitals, mass pharmaceutical dispensing sites during severe epidemics) and mass transit areas (e.g., airports, train stations, bus stations) where infectious travelers could harbor influenza and other febrile diseases.

In step with the World Health Organization's *International Health Regulations* guidance, the Department of Homeland Security's *One-Health Approach to Influenza* recommendations, and the United States Department of Health and Human Services' *National Health Security Strategy* vision, there is still an unmet requirement to monitor for emerging and reemerging infectious diseases by augmenting the global capacity for disease surveillance, detection, rapid diagnosis, and reporting (Powdrill, Nipp, & Rinderknecht, 2010; United States Department of Health and Human Services [USDHHS], 2009; World Health Organization [WHO], 2005a). If proven effective for the identification of febrile (ill) subjects, IRT could be used to rapidly detect potentially infectious individuals before they come in contact with another susceptible population, which could reduce the disease burden attributed to influenza. This reduction could result in positive social change by further supporting public health and the previously mentioned global regulation and federal guidelines.

IRT could be perceived as an intrusive or beneficial surveillance tool depending how it is utilized, reported, and publicized. By thoroughly exploring this technology, addressing its strengths and limitations, and informing the public of its benefits, positive social change through education can be achieved. Additionally, senior decision makers in both civilian and military public health will be further supported by having the ability to make an informed decision on the future use of IRT.

Summary and Transition

This chapter highlighted the public health importance of adequate surveillance: early detection and reporting of biological threats and the federal and global regulations that call for increased public health vigilance through increased surveillance measures. Additionally, chapter 1 introduced the problem statement, research questions and hypotheses, significance of IRT research inquisition, definition of terms, and the assumptions and limitations within the IRT literature.

Chapter 2 provides the background information on IRT, ILI, public health surveillance, and the literature related to the research question, hypotheses, the problem statement, and objectives of the current study. More specifically, this chapter will compare and contrast the IRT literature while covering the historic applications of IRT, protocol for using these cameras, materials that may impede infrared emittance, the physiologic response of fever that could dupe IRT screening, environmental influences affecting IRT measurements, and the various types of IRT equipment. Finally, chapter 2 ends with a discussion of the methods used in past IRT research that apply to this study.

Chapter 3 provides further details with concern to the methodology utilized to investigate the efficacy of fixed IRT for identification of subjects with ILI. This chapter

includes a description of the research design and approach, an understanding of the sample population with justification of the sample size used, diagnostic measures used to confirm disease exposure, and the screening equipment and procedures used by the public health team.

Chapter 4 is centered on the research questions and hypotheses constructed for this study. It covers the data collection instruments, IRT standard operating procedures, and a presentation of the analyses through interpretation and explanation of the statistical findings. Chapter 5 begins with a brief overview of the purpose and methods of this study, reviews the research questions, and interprets the findings. Additionally, the chapter includes conclusions that address all the research questions and are formulated from the results in the previous chapter. It concludes with recommendations for future IRT studies, potential researcher biases, and implications for social change.

Chapter 2: Literature Review

Introduction

The primary intent of this review is to provide background information on infrared thermography (IRT), influenza-like illness (ILI), and public health surveillance. This review compared and contrasted the IRT literature (including technical manuals and manufacturer guidelines) with particular attention to IRT equipment, protocols for using these cameras, environmental conditions that skewed IRT readings, materials that impeded infrared emittance, IRT operator threats to internal validity, and optimal thermal target zones for IRT screening. All of these factors were explored in terms of IRTs potential role in public health, specifically in identifying emerging and reemerging ILI biological threats.

Methods for execution of this literature review included searching peer-reviewed and academic literature from computerized databases and resources: ABI/INFORM Global, Academic Search Premier, Encyclopedias from Sage, eBrary e-book collections, Education Research Complete, Expanded Academic ASAP, General Science Collection, Health and Medical Complete (ProQuest), Health Sciences: a Sage Full-Text Collection, IEEE Xplore Digital Library, InfoSci Journals, Cumulative Index to Nursing and Allied Health Literature (CINAHL), MEDLINE with Full Text, Military and Government Collection, ProQuest Central, ResearchNow, Science Direct, SocINDEX with Full Text, and applicable academic textbooks. The following keywords were used alone and in combination as search terms: *fever, febrile, screening*; *noncontact infrared thermography*; *infrared thermal detection system*; *infrared thermography*; *infrared thermograph*; *infrared thermometry*; *thermal imaging*;

pyrometer, pyrometry; *thermal screening*; *influenza like illness*; *public health surveillance,* and; *syndromic surveillance*. The evident redundancy in terms was needed because a standardized vernacular has not been established for this technology. Only text in English was reviewed, with most literature published between 2003 and 2010, which was limited to approximately 15 research studies as IRT is a newly utilized technology in public health. Of note, the 2003 severe acute respiratory syndrome (SARS) epidemic in Asia was a significant impetus for continued IRT research and this research significantly contributed to IRT methodology, limitations, assumptions, and conceptual framework.

Conceptual Framework

As introduced in chapter 1, the conceptual framework for IRT research was derived from three areas throughout the IRT literature: (a) environmental influences that affected IRT measurements, (b) highest thermal yield anatomical region for IRT screening, and (c) IRT correlation to aural and oral measurements. These areas of focus are the foundational studies that explored the efficacy of IRT; however, this framework is limited in scope as the utilization and research of this technology in public health screening has only been around approximately seven years. Nevertheless, these areas provided a conceptual and guiding framework for the focus of this study (see Figure 1). First, environmental influences such as humidity, excessive room temperature, and wind turbidity have been suggested to affect IRT measurements (Chan et al., 2004; Chiang et al., 2008; Chiu et al., 2005; Ng et al., 2004; Ng et al., 2005; Nguyen et al., 2009; Ring et al., 2008). If environmental influences are not controlled

then IRT efficacy when screening will diminish as a result and will be further discussed in greater detail in this chapter. Second, Ng et al.'s (2004) research focused on the medial canthus as the region that emits the highest thermal yield and was further supported in other studies and a technical reference (viz., Chiu et al., 2005; ISO, 2008; Ng et al., 2005, Ring et al., 2008). By honing the IRT to this region during screening, the surface temperature will more closely mimic that of the core temperature, and efficacy of this technology will be increased due to increase reliability and accuracy with relation to clinical thermometry Third, the literature demonstrated IRTs ability to function as a proxy to clinical thermometers and to differentiate between normal temperature and elevated temperature subjects (Chan et al., 2004; Chiang et al., 2008; Liu et al., 2004; Ng et al., 2004; Ng et al., 2005; Nguyen et al., 2009; Ring et al., 2008). Accordingly, those findings validated IRT as a comparable temperature gathering device with comparison to clinical thermometry. These three areas within the IRT literature all lend to IRT efficacy, with the understanding that the main objectives of this technology are to rapidly and accurately parallel oral/aural thermometry readings to identify febrile subjects. Consequently, the three focus areas mentioned in this section provided the framework for this study and will be further discussed in this chapter along with other categories that contributed to the further exploration of the efficacy of fixed IRT for the identification of subjects with ILI.

ILI

ILI is a term used to describe fever (≥ 100°F) and cough and/or an irritated throat in the absence of a known cause other than influenza (Centers for Disease Control [CDC], 2010h). Its symptoms are the key alert factors that public health officials use to monitor for infectious diseases entering the United States borders (CDC, 2009j). ILI is a nonspecific term used during screening; follow up confirmatory diagnostics are then conducted to identify the actual pathogen. Some of the recent ILIs that have caused epidemic and pandemic disturbances have been: influenza, parainfluenza (PIV), coronavirus (e.g., SARS), and adenovirus (Apisarnthanarak et al., 2010; CDC, 2010c; CDC, 2010d).

Of the above mentioned infectious diseases a particular virus is of utmost concern. This concern is due to the remarkable epidemiological characteristics and fickle nature of the influenza virus. Generally, its annual emergence causes attack rates of 10% to 30% globally (Steinhoff, 2006). Influenza is responsible for approximately 200,000 hospitalizations and 36,000 deaths per year in the United States (CDC, 2010a). The global mortality rate is estimated between 250,000 to 500,000 cases per year with an approximated morbidity rate between three and five million cases per year (World Health Organization [WHO], 2010). More specifically, influenza is a virus of pandemic potential. Its threat is generated due to its lack of proofreading during replication that facilitates antigenic drift (minor antigenic change) and antigenic shift (major change in surface antigens). Its zoonotic nature (transmitted from animals to people) that contributes to genome variation provides a viral survival advantage (more hosts to

infect), and viral mobility (avian dispersal) that may all culminate in a novel strain with pandemic potential (Steinhoff, 2006).

The 2009 H1N1 virus was an example of a novel emerging influenza strain that caused a pandemic (CDC, 2010i). This novel emerging strain was responsible for causing infection in more than 214 countries and territories worldwide and for over 18,449 attributed deaths; it continues to be a dominant strain in the 2010 Southern Hemisphere flu season (WHO, 2010b). Additionally, recent evidence suggested those infected with the 2009 H1N1 virus had the common symptoms of fever (93%) and cough (83%; CDC, 2010i). The occurrence of this recent pandemic reinforces the need for increased and continual surveillance for influenza viruses specifically, and ILIs more generally, in order to attenuate their burden on health (Powdrill, Nipp, & Rinderknecht, 2010; WHO, 2005a).

Surveillance and IRT

Surveillance is the focused awareness of behaviors, activities, and atypical and typical patterns of individuals in a candid observation (O'Carroll et al., 2003). This observation in the public health arena extends into a subcategory called syndromic surveillance, which is the utilization of health-related data that precedes a diagnosis to indicate the likelihood of an infectious case or potential outbreak (O'Connell et al., 2010). Syndromic surveillance can take many forms, from collation and filtering of data from disease registries to algorithmic interpretation of reports from mass entry checkpoints. Some of these checkpoint reports are created from self-report health status questionnaires completed by travelers, vessel and airline crews notifying quarantine stations of suspected ill passengers, and passive and active screening of travelers'

temperatures while entering international checkpoints. A potential method to passively screen travelers' temperature is through the use of IRT.

Applications of IRT

The discovery of infrared radiation was first attributed to the German astronomer William Herschel before the Royal Society of London in 1800 (Jones, 2010). Since that time, several discoveries, theorems, laws, and technological advancements have facilitated the expansion of this portion of the electromagnetic spectrum to be visualized on film and in real-time video. The first film imagery appeared in the 1950s from the work of Paul Kruse with collaborative efforts of Honeywell and Texas Instruments, which captured hyper thermal regions within electric circuitry (Bhattacharya et al., 2002; Jones, 2010). It was not until 1965 that the first commercial grade imager was produced by FLIR Systems Incorporated that was primarily used for industrial system scanning. Since this period, IRT has grown in popularity and scope and now has a litany of commercial and private uses (Bhattacharya et al., 2002).

Some of the most common applications of IRTs are used in aerial scanning to illustrate the environmental impacts associated with drought conditions, electrical and mechanical preventive maintenance to check for electrical inefficiencies and possible fire hazards, in security to enhance night vision capabilities, and an array of applications within the medical field (Blum, Farrier, & Leando, 2003;Infrared thermometers, 2010). More specifically, medical relevance of IRTs screening capacity includes recognition of: breast pathologies, extra-cranial vessel disease, perfusion abnormalities, neuro-musculo-skeletal dysfunction, digestive disorders, and lymphatic dysfunctions (Bagavathiappan et al., 2009). Another possible medical use of IRT is in identifying febrile subjects that

might be harboring communicable disease. Specifically, IRT may be a useful screening tool for public health practitioners at mass points of embarkation, debarkation, schools, large office complexes, and hospitals to help attenuate the annual burden of disease attributed to influenza, as IRT can identify the elevated heat signature from febrile subjects (Ng et al., 2005; Nguyen et al., Ring et al., 2008).

Causes of Elevated Body Temperature

The premise behind using IRT for identifying febrile individuals for possible infectious disease is due to the body's physiological response to antigens entering the body that may cause illness. Pyrexia, more commonly known as fever, is a temporary elevation of the body's typical thermoregulatory homeostasis which usually fluctuates between 1-2 °C (Marieb, 2001). While IRT can identify the elevated heat signature of a febrile subject, this elevated temperature is not always indicative of infectious disease and must be further explored.

Commonly, the average human oral body temperature ranges between 36.1°C and 37.5°C (96.9°F - 99.5°F). Nevertheless, there are a multitude of fluctuations in a normal body temperature (not influenced by infectious disease) that can be the result of fasting, consumption of hot or cold liquids, general exertion level, various points within the menstrual cycle, pregnancy, alcohol consumption, antipyretic medications, hormonal therapy, time of day, and even a postprandial relationship (Chiang et al., 2008; Marieb, 2001; Ng, 2004). The lowest body core temperature is around 4 a.m., while the peak occurs around 6 p.m., given a typical work and rest circadian sleep cycle (Marieb, 2001).

Following this further, pyrogens are fever-producing substances that may be in the form of viruses, bacteria, fungi, toxins, or even pharmaceuticals – not necessarily

infectious materials (Harrisons Internal Medicine, 2008). These substances stimulate the release of prostaglandin E2 (PGE2) a hormone that acts upon the hypothalamus, the temperature regulatory center of the brain, which elevates the thermoregulation of the body. A product of this regulation is increased muscle tone (shivering) and vasoconstriction (to conserve heat loss) that ultimately raises the body core temperature (Harrisons Internal Medicine, 2008). Elevated body temperature is marked by four temperature grades: low grade, 38-39°C (100.0-102.2°F); moderate, 39-40°C (102.2-104.0°F); high-grade, 40-41.1°C (104.0-105.98°F); and hyperpyrexia, > 41.1°C (>105.95°F; Harrisons Internal Medicine, 2008). This newly acquired thermal set-point, that may or may not indicate infection, is maintained until PGE2 is no longer present. Nevertheless, elevated body temperature remains a cardinal indicator of ILI and this elevated heat signature is what IRT uses to differentiate between febrile and afebrile individuals and will be further examined in the next section (CDC, 2010c).

IRT and Selection of Febrile Subjects

IRT is a system that converts infrared (IR) energy (i.e., heat) into an image through sensors that are responsive to this spectrum. As a result, higher IR emittance regions (e.g., medial canthus of the body, as explained in the thermal target zone section, below) further stimulate these sensors to produce a specific electronic impulse, which is then converted into a signal that correlates to a color on a monitor, while lower emittance regions also produce a specific impulse in accordance with the lowered stimulus. The end result is a polychromatic, real-time visualization of the temperature variations within the camera's field of view (ISO, 2008). In addition, the maximum acquired temperature is displayed and a threshold temperature can be programmed to sound an alarm if a set

temperature is exceeded. Thus, individuals with fever would be identified both visually and audibly to the operator (see Figure 2).

Figure 2. Example of a febrile subject thermogram.

Because IRT technology can identify elevated surface temperature in human subjects, it has the potential to play an important role in syndromic surveillance. Syndromic surveillance, as previously discussed, is the recognition of symptoms, behaviors, and other health-related data that precede diagnosis. As such, IRT can help to determine whether or not a febrile subject has ILI by objectively and passively mass screening a population for the symptom of fever, which cannot be easily or quickly completed using conventional oral and aural thermometry devices. Once identified as febrile, public health officials can further assess the individuals for ILI, seek diagnostic confirmation if warranted, report disease if confirmed, take appropriate steps to treat and isolate any infected individuals, and conduct outbreak investigations as necessary in order to reduce transmission of the disease. In order for IRT to be an integral part of syndromic surveillance and identify febrile individuals, there are many parameters that need to be

considered when using this technology, one of which is an appropriate temperature threshold.

Temperature Thresholds for IRT

Threshold limits are established to alert the IRT operator of subjects who are near or exceeding a predetermined surface temperature. Due to the inaccuracy (approximately +/- 1°F) of the IRT equipment, a threshold temperature below that of a low grade fever is typically chosen (ISO, 2008). For instance, in a meta-analysis of fever screening studies by IRT from 2004-2008, temperature threshold limits for the included studies ranged from 36.3°C to 38.0°C (97.3°F to 100.4°F; Bitar et al., 2009). Some IRT researchers have addressed threshold temperatures in their studies in order to establish the parameters for an optimal setting.

A fundamental IRT study completed by Ng, Kaw, and Chang (2004) helped to establish a model temperature threshold limit. In this study, a sample of 310 subjects were all screened with IRT (independent variable) and then their oral temperatures (dependent variable) were taken. The sensitivity and specificity of those temperatures were compared to various threshold temperature levels ranging from 33.0°C to 37.0°C. The intent was to find the highest values of both sensitivity and specificity for threshold temperatures from the cohort being screened. Notably, this study did not test temperatures over 37°C as the lowest tradeoff between sensitivity and specificity was reached at 36.3°C. Nonetheless, as the threshold temperature diminished (e.g., 33°C) the sensitivity reached 100% (95 % confidence interval [C.I.], 92.5 - 100.00), but at the expense of specificity that dropped to 0.0% (95% C.I., 0.0 - 1.4). At the other extreme, as the threshold temperature was raised to 37°C the sensitivity was reduced to 66.7%

(95% C.I., 51.6 – 79.6) and specificity was raised to 99.6% (95% C.I. 97.9-99.9). The optimal temperature to maximize sensitivity and specificity was determined to be 36.3°C, which resulted in 85.4% sensitivity (95% C.I., 72.2 - 93.9) and 95.0% specificity (95% C.I., 91.7 - 97.3; Ng, Kaw, & Chang, 2004).

Other IRT studies have used slightly different (i.e., +/- 0.5°C) threshold temperatures (e.g., Chiang et al., 2008; Chiu et al., 2005; Hausfater et al., 2009; Liu et al., 2004). These minimal differences in threshold temperatures were most likely not meaningful as different IRT models were used throughout these studies, core-to-surface adjustments could have varied, and environmental factors that can affect the establishment of a threshold limit may have differed (Nguyen et al., 2009). What defined Ng, Kaw, and Chang's (2004) study were their descriptive methods of how they established the highest yielding threshold from use of specificity and sensitivity measurements. The other studies merely listed threshold temperatures without defining how they were achieved.

As touched upon previously, threshold limit temperatures are specific to the IRT system used and possibly affected by environmental factors (see below), so this threshold must be tailored to each IRT to ensure an effective limit (Chiang et al., 2008; Ng et al., 2004; Nguyen et al., 2009). Table 1 summarizes three IRT studies that address threshold temperatures. The studies had various optimal threshold temperature results, which may be attributed to the differing IRT equipment used in those studies and environmental influences affecting measurements (viz., humidity, temperature extremes, air turbidity); comparison of these studies further highlights how threshold temperature is specific to the equipment and the setting (ISO, 2008).

Table 1

Review of Temperature Threshold Limits: IRT Studies

Reference	Objective(s)	Equipment	Sample Size	Methodology/ Analysis	Results	Conclusions & Limitations
Ng, Kaw, & Chang (2004)	To investigate forehead vs. inner canthus in relation to core temp., & ideal threshold temp.	IR ThermaCAM S60 FLIR system, uncooled, thermal sensitivity of .08°C @30°C, fixed IR model	n=310	1) Focal length from subject to scanner was 2m, scan time per subject 2 sec. 2) Study conducted indoors, Singapore Hospital ER, Emissivity used .98, subjects in study derived from ER triage 3) Regression analysis, ROC Curve analysis, sensitivity & specificity 4) Convenience sample from one hospital	1) Ideal threshold limit was 36.3°C (sensitivity 85.4% & specificity 95.0%) 2) Medial canthus highest thermal yield (r^2=0.55); forehead (r^2=0.49)	1) IRT showed favorable results for mass blind screening when medial canthus was selected w/ correlation to aural temperature. 2) Preset threshold temp est. for 36.3°C, temps exceeding this reading will trigger alarm & secondary screening to follow
Chiang et al. (2008)	To investigate threshold limits and optimal screening distance	Digital Infrared thermal imaging (DITI), spectrum 9000MB Medical Thermal Imaging System, cooled, thermal sensitivity of .08°C @30°C, 60 frames per sec., fixed IR model	n=1032	1) Focal length from subject to scanner was 0m, 5m, and 10m 2) Study conducted indoors, in an ER in Taipei, Taiwan, emissivity not listed, study participants derived from ER triage 3) Regression analysis, ROC, sensitivity and specificity, false positive and false negative rates, positive predictive value (PPV) 4) Convenience sample from one hospital setting	1) ROC analysis showed optimum threshold temperature to be 36.25°C 2) Sensitivity at 0m was 13%, specificity 95%, PPV 44%; sensitivity at 5m was 45% and specificity was 70%, and PPV 29%; sensitivity at 10m was 57% and specificity 85%, PPV 39%	1) Preset threshold temp. of 36.25°C 2) Human surface temperature correlated with core body temperature 3) Favorable results for mass, noncontact screening 4) Notable ambient temperature discrepancy that affected measurements 5) DITI may produce false-negatives 6) Sensitivity reduced if subject is sweating

(*table continues)*

Reference	Objective(s)	Equipment	Sample Size	Methodology/ Analysis	Results	Conclusions & Limitations
Hausfater et al. (2008)	To assess the diagnostic accuracy of infrared thermometry for detecting patients with fever	Raytek Raynger MX2 Infrared Thermometer (industrial grade), no image display, uncooled system, hand held model	n=2026	1) Distance from subject to scanner was not listed, hand held IR unit 2) Study conducted indoors at a hospital in France, did not mention adjustable emissivity 3) ROC used for threshold temp., multivariate regression analysis between tympanic and infrared measurements, sensitivity and specificity, PPV, NPV 4) Fever was listed as >38.0°C 5) Convenient sample from one hospital	1) ROC analysis showed optimum threshold temperature to be 38.5°C 2) Sensitivity at ≥38.5 was 82%,specificity was 90%; PPV 13%, NPV 100%	1) Threshold limit of 38.5°C 2) Sensitivity lower than expected, low PPV 3) Age as a variable that interferes with cutaneous measurements with IR 4) Infrared thermometry does not reliably detect febrile patients due to low sensitivity and PPV

Validity, Accuracy, and Reliability of IRT

Validity and reliability of the use of IRT have been debated since its incorporation into the public health domain for screening of febrile individuals for ILIs. Although mass remote screening with IRT has not been widely used in the United States, its applications have been extensively tested in international airports, rail stations, and hospitals throughout Asia and parts of Canada (Bitar et al., 2009). From these gathered studies, the validity of IRT to identify febrile individuals in terms of sensitivity, specificity, and predictive values will be explored; additionally, the accuracy and reliability (repeatability/precision) of IRT with relation to differing equipment will be summarized.

Sensitivity and Specificity

It is important to note sensitivity and specificity in the IRT literature does not follow the typical public health exposure versus disease model. Rather, sensitivity in current IRT studies is indicative of subjects exceeding an established threshold limit (triggering an alarm from the thermal scanner; which may be considered the exposure) and then having a secondary temperature confirmed from a standardized clinical thermometer (assumed disease), which would indicate a true positive. This value is divided by all subjects who presented with fever upon secondary temperature screening, yet were not detected by IRT (false negative), and those whom exceeded IRT threshold limits and presented with secondary temperature (true positive) from a standardized thermometer. A comparable set of measures is used to calculate specificity.

Both sensitivity and specificity can be used to show the effectiveness of a screening tool such as IRT, and there is debate over the ideal balance between these

measures. One view is that for a mechanism that is attempting to mitigate potentially infectious individuals from integrating within a susceptible population, the goal should be high sensitivity, even at the cost of diminished specificity, for the sole purpose of minimizing false negatives (Ng, 2004). The way to achieve high sensitivity in IRT studies is to reduce the threshold temperature slightly below that of a low grade fever (Chiang et al., 2008; Ng et al., 2004). By doing so, slightly abnormal thermal subjects will be identified and, by standardized operating procedures, subjected to follow-up screening, health questionnaires, or interviewed to rule out the potential of harboring infectious disease in those subjects. Although this additional screening will have a negative effect on specificity as more subjects (false positives) will be identified without probable infection, fewer false negative subjects will be introduced into a susceptible population as a result.

Not everyone agrees that high sensitivity should be the goal for IRT screening. It has been proposed that relatively high threshold temperatures ($\geq 37.5°C$) should be favored in mass screening using IRT to avoid false positives (Mercer & Ring, 2008), presumably for the purposes of maintaining high specificity. However, the main purpose of using IRT as a sentinel surveillance tool is to identify potentially infectious individuals and sequester them from the vulnerable populous. For this reason, false positives do not pose a significant limitation of the system because those with borderline febrile conditions must have a secondary screening to rule out fever (Chiang et al., 2008). IRT is merely one layer of protection that offers the capability to rapidly mass screen individuals for fever. As such, sensitivity must remain heightened to avoid minimally

subclinical subjects being undetected (false negative) in this primary, but not final screening process (Ng et al., 2004; Cheung et al., 2008).

Although high sensitivity may be preferable, not all IRT studies of the detection of febrile subjects have met this goal. Bitar et al. (2009) examined IRT screening at mass collection points through a meta-analysis using a MEDLINE search to explore the literature from 1975 to 2008 under the following key words: fever; screening; noncontact; infrared thermography; thermal imagers; pyrometry; thermal screening (see Table 2). Bitar et al.'s (2009) literature summarized high specificity (94 to 99.6%) and high negative predictive values (91 to 99%) when using IRT for detection of febrile subjects, along with low sensitivity (67 to 89.6%) and low positive predictive values (69.9 to 81.4%) – values not high enough for either sentinel awareness or monitoring of false negatives (Bitar et al., 2009).

Although Bitar et al.'s (2009) research provided a collective review of modern IRT studies addressing the detection of febrile individuals, the studies themselves had several shortcomings, particularly with regards to the equipment used. One criticism of the meta-analysis is that Bitar et al. (2009) did not compare and contrast the infrared equipment used in the various studies, which is a major foundation for assessing the efficacy of IRT (see Table 2). Infrared thermal temperature readings can be gathered through an assortment of equipment types, as mentioned throughout this chapter, but specific equipment is needed to account for the confounding variables of skin emissivity, ambient temperature, facial targeted zones, multiple-zone thermal gathering, and core-to-surface corrections to increase the recognition of true positive febrile subjects (Ng, 2004; Liu et al., 2004; Chiu et al., 2005). Two of the six infrared thermometry devices used in

the studies reviewed by Bitar et al. (2009) were industrial IR scanners designed for preventive maintenance applications, such as identifying electrical hot spots and thermal loss in various materials. These industrial units have a fixed emissivity ($\varepsilon = 0.95$) that relates to such materials as limestone and white marble, not human skin (Table of Total Emissivity, 2010). Consequently, IRTs with fixed emissivity can potentially detect both reflected and emitted IR signatures that are not a true representation of the scanned surface temperature (Giancoli, 1998). Thus, inaccurate surface temperatures may have been detected in the IRT studies reviewed in the meta-analysis.

In addition to fixed emissivity, the two industrial infrared thermometers in the Bitar et al. (2009) meta-analysis had other limitations. These scanners did not have multiple-zone thermal gathering capabilities that screen the entire field of view for the highest thermal readings, they could not be calibrated for ambient temperatures, and they are point-and-shoot scanners that have laser targeting to indicate the scanned region; hence for the sake of safety, they could not be used in the ocular region (highest thermal yield) due to possible retinal damage. There were also other equipment concerns in the various studies reviewed. One of the four medical grade IRTs lacked adjustment for ambient temperature, skin emissivity, and required the operator to be within inches of the subject to gather a reading – thus increasing potential spread of disease to operator. Additionally, this product takes longer than medical grade IRT devices to acquire multiple readings, which is not optimal; likewise, it is not marketed through the manufacturer for mass screening use in human fever detection (ISO, 2008).

Many of the IRT devices used in the studies reviewed by Bitar et al. (2009) were merely designed to interpret infrared radiation from an inanimate object; in contrast, IRT equipment designed for human fever detection has precise settings and calibrations to increase accuracy when imaging and screening for fever in humans (Mercer & Ring, 2008). Bitar et al.'s (2009) conclusions need to be considered with the caveat that dissimilar, medical-grade (specifically designed for human fever detection), or industrial IRT equipment were compared without mention of the limitations or superiority of equipment for recognition of elevated infrared surface temperatures in humans. Likewise, these implications must be noted as a potential instrumentation threat to internal validity within IRT studies because the use of nonmedical grade equipment may weaken the argument that the independent variable (core temperature) was exclusively liable for the observed effect (surface temperature; McMillan, 2004).

Another example of how nonmedical grade IRTs can alter IRT sensitivity and specificity may be observed in the Hausfater et al. (2008) study. In this study, Hausfater et al. (2008) revealed marginal sensitivity (82%) and low positive predictive value (77%) with the use of IRT for detection of febrile subjects (see Table 2) in a convenience sample of 2,026 subjects (57% male, 43% female) who were admitted to the emergency room of the Pitie-Salpetriere University Hospital in Paris, France. The independent variable was core temperature assessed by medical-grade tympanic thermometers and compared to the dependent variable, surface temperature, that was acquired from the frontal cephalic region (forehead) using the Raytek Raynger MX2® (industrial grade) Infrared Thermometer. The forehead region was selected based upon guidance from past IRT research studies (Ng, Kaw, & Chan, 2004; Ng et al., 2005). The surface temperature

threshold limit was established using receiver operating characteristic (ROC) analysis (IRT readings to predict medical-grade tympanic [aural] thermometer readings) and determined to be 38.0°C/100.4°F (ROC curve was 0.87 [95% CI 0.807-0.917, $p<0.01$]). This threshold limit was elevated (~ 1°C higher) compared to limits in other IRT studies (see Figure 2), and may have also contributed to the low sensitivity of this study (Chiang et al., 2008).

Hausfater et al. (2008) asserted that the use of basic infrared thermometers (industrial grade) versus medical grade infrared thermographic imagers should not be considered as a limitation when screening for febrile subjects as their findings could be extrapolated to any device that estimates surface temperature (Hausfater, 2008). However, their study was not guided by past IRT research successes and limitations in terms of appropriate equipment to use, adjustments for emissivity, and ambient environmental temperature as the equipment used in the study was an industrial grade IRT that could not be adjusted to account for these variables. Nonetheless, Hausfater et al.'s findings suggested that IRT was not a reliable tool for screening of febrile individuals due to high false positive rates and low positive predictive values associated with this equipment. While appropriate IRT equipment is necessary to achieve high sensitivity and specificity during measurements, the accuracy of this equipment must be further explored.

Accuracy

The accuracy of a system is the degree of proximity of a measurement to its actual value, or in the case of IRT, the ability to distinguish between an afebrile individual and a febrile individual (MedCalc, 2009). The information to obtain sensitivity and specificity is based on IRT acquired surface temperature versus oral temperature from that same subject, thus the clinical thermometer reading (oral temperature) establishes how close or far away the IRT reading is to this actual value. Through ROC analysis (see figure 3), which is a plot of true positive rates versus false positive rates a graphical means of comparison between afebrile and febrile individuals can be illustrated (Ng et al., 2004; Shapiro, 1999). Ng et al. (2004) conducted ROC analysis, by studying the area under the curve (AUC), which suggested randomly selected febrile (positive) subjects have test values larger than that of an indiscriminately selected afebrile (negative) subject 97.2% of the time (95% CI = 0.947-0.987; see Table 2) .

These results were similar to Nguyen et al.'s (2009) conclusions. In that study Nguyen et al. compared three different medical grade IRT cameras (see Table 2). The selection process for the IRT equipment was based on requiring equipment specific for fever screening (i.e., camera field view, sensitivity focus characteristics, temperature range, tripod mount, operational distance, and calibration standards); cameras were obtained through a competitive bidding process (Nguyen et al., 2009). Notably, the selection process did not mention guidance from the international standards for IRT screening of human febrile subjects (e.g., ISO, 2008), which highlights equipment specifications. Nevertheless, Nguyen et al.'s (2009) results suggested that the

OptoTherm IRT had the highest ROC (AUC) of 96.0%, followed by the FLIR (92.1%), and Wahl (78.8%) – notably these are all comparable medical grade IRTs and meet ISO requirements. Consequently, Nguyen et al. discussed that the Wahl IRT might have had a lower AUC as this IRT needed to be calibrated for ambient temperature each day with the assumption that room temperature would remain constant. However, room temperature did not remain constant (as shown in their data logs) and the IRT was not recalibrated to accommodate the temperature fluctuations (Nguyen et al., 2009). Therefore, with the exception of the Wahl IRT, these results suggested that IRT has the capacity to differentiate between febrile and afebrile subjects. Additional studies demonstrating IRTs accuracy are necessary as limited research exists to support these conclusions.

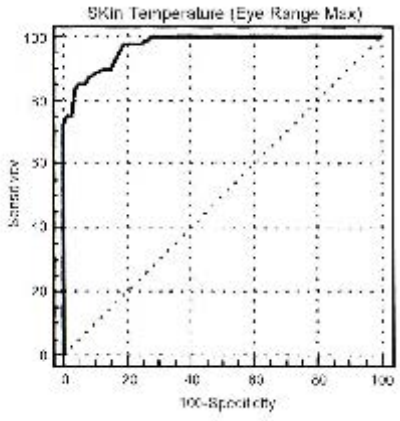

Figure 3. Example of a ROC plot. *Note*. The ROC plot is from "Analysis of IR Thermal Imagers for Mass Blind Fever Screening," by Y. K. Ng, G. L. Kaw, and W. M. Chang, 2004, *Journal of Microvascular Research*, *68*, p. 107. Copyright 2004 by Elsevier Inc. Reprinted with permission.

Reliability

Sensitivity, specificity, and accuracy are helpful measures of system effectiveness; nonetheless, if a test cannot be repeated the usefulness of the test is minimal (Gordis, 2004). Two factors continually convolute IRT equipment reliability and threaten internal validity: intra-subject variation and inter-observer variability. To avoid these threats, a standard operating procedure (SOP) must be established, followed, and reviewed to minimize inter-observer variability, which is achieved by temperature measurements taken by only one examiner. If this is not possible, multiple operators must be properly trained on the IRT equipment and follow a SOP to ensure similar interpretations of the IRT measurements are made regardless of the operator (ISO, 2008). In addition, intra-subject variation must be minimized by controlling environmental variations (viz., maintaining comfortable room temperature & humidity) and using a prescreening questionnaire covering antipyretics, exertion, time of day, and last oral intake (i.e., hot fluids & food; Chan et al., 2004; Ng et al., 2004; Mackowiak et al., 1992).

Potential IRT Covariates

Certain factors may pose significant threats to validity, accuracy, and the reliability of IRT surface temperature measurements by acting as confounders or effect modifiers. Throughout the IRT research literature various covariates have been discussed; however, these covariates were addressed in the discussions rather than included as variables in the studies. Only a few variables have been included in IRT studies and critically assessed as covariates. For example, Chiu et al. (2005) found perspiration to be a significant variable that may produce false negatives and decreased IRT sensitivity, as this physiological response reduces the surface temperature; however,

the actual temperature reduction was not listed in their findings (see Table 2). Hausfater et al.'s (2008) research, which included participants between the ages of 6 and 103, identified age as a covariate affecting IRT readings. However, Hausfater et al. merely mentioned that geriatric participants (age not defined) showed instability of core temperatures during alternation of cold and heat conditions (see Table 2). This was an assumption made as thermoregulatory decline is a typical function of senescence (Degroot & Kenney, 2007), yet Hausfater et al. did not show any analysis of temperature variation in their results to support this finding. Nguyen et al. (2009) identified gender as a possible covariate as the male average surface temperatures were slightly higher (0.2°F) than female surface temperatures on all three IRT cameras used in their study. Nguyen et al.'s conclusion was that gender differences in body fat, hair, or facial cosmetics could jointly or alone affect IRT readings. Furthermore, certain medications, exertion, and intake of hot and cold fluids are all potential covariates, previously mentioned under the Physiology of a Febrile Response section; because they affect core temperature measurements that may in turn affect IRT measurements (Marieb, 2001). Other covariates related to environmental conditions and IR impeding materials will be later discussed in this chapter.

Although specific variables pose threats to validity, accuracy, and reliability it should be noted that not all ILI infections result in elevated temperature. Subclinical (inapparent) infection has been recognized as a potential threat to public health because host viral shedding could be occurring without the recognizable symptom of fever (Cheung et al., 2008; Ng et al., 2004; Sompayrac, 2002). In contrast, hyperthermia, which is a long-term increase in body temperature due to excessive heat production or

inadequate thermoregulation, could be another condition that causes fever, but not as an indicator of ILI (Mackowiak et al., 1992). These alternative causes of elevated temperature further demonstrate the need for additional measures after IRT screening to rule out ILI.

In summary, the validity, accuracy, and reliability of IRT measurements could significantly be jeopardized due to the effects of covariates. Above all, the value of addressing covariates in IRT studies is to explain potential limitations with this equipment, and they must be measured whenever possible. In addition, accounting for certain covariates (i.e., IRT equipment, environmental influences, and IR impeding materials) could increase the validity, accuracy, and reliability of IRT measurements in comparison to oral thermometry (Bendiganavale & Malshe, 2008; ISO, 2008; Ng et al., 2004; Ring et al., 2010). The next section will discuss the thermal target zones that may be considered when screening subject with IRT devices to acquire the highest thermal yield.

Table 2

Review of Literature: IRT Studies from 2004-2009

Reference	Objective(s)	Equipment	Sample Size/Variables affecting measurement	Methodology/ Analysis	Results	Pros / Cons
Ng E et al. (2004)	To investigate forehead, eye, inner canthus in relation to core temp., & ideal threshold temp.; proxy to clinical thermometers	IR ThermaCAM S60 FLIR system, uncooled, thermal sensitivity of .08°C @30°C, fixed IR model, adj. emissivity, adj. for ambient temp., medical grade; spectral range – long wave; focal plane array, accuracy +/- 2°C, range -40-1500°C	1) n=310 2) Ambient temperature affecting IRT readings	1) Focal length from subject to scanner was 2m, scan time per subject 2 sec., forehead & medial canthus screened 2) Study conducted indoors, Singapore Hospital ER, Emissivity (ε) used .98., subjects in study derived from ER triage 3) Sensitivity, specificity, regression, ROC analysis 4) Eye glasses affecting IRT reading 5) Data from SARS epidemic in Singapore	1) Ideal threshold limit was 36.3°C by ROC analysis (sensitivity 85.4% & specificity 95.0%) 2) Medial canthus (frontal cephalic [FC]) highest thermal yield (R^2=0.55); forehead (R^2=0.49); eye (R^2=0.0622) 3) Contact lenses not affecting IRT reading 4) ROC/AUC 97.2% (95% C.I.=0.947-0.987)	1) Pros: Optimal anatomical region to screen; perspiration lowering surface temperature; est. of ambient temp range; medical grade equip. that can adj. for emissivity, core-2-surface, ambient temp., fixed IRT 2) Cons: SOPs not listed

(*table continues)*

Reference	Objective(s)	Equipment	Sample Size/Variables affecting measurement	Methodology/ Analysis	Results	Pros / Cons
Liu et al. (2004)	Study the efficacy of IR screening as a proxy to clinical thermometers; highest yield anatomical region	Thermofocus Thermometer, Tecnimed, Italy, IR thermometer; w/out camera, focal length, no emissivity adj., ambient temp., or surface-to-core; spectral range – short; accuracy +/- 0.3°C; range- 34-42.5°C	n=500	1) Forehead measurement, approx. 1 inch., scan time per sub. 2 sec. 2) Study conducted outdoors, Taiwan Hospital ER, no emissivity used 3) Sensitivity, specificity, regression, ROC analysis 4) Data from SARS epidemic in Taiwan	1) Threshold temp. 37.5°C 2) Highest thermal yield: auditory meatus (AM) (r=.56), FC (r=.25); AM sensitivity (82.7%), FC (17.3%), AM specificity (98.7%), FC (98.2)	1) Pros: all measurement taken by single operator; SOPs used 2) Cons: screening outdoors, nonmedical grade IR equip., equip. required operator to be within inches of possibly ill subjects; equip. could not be adj. for emissivity, core-2-surface, ambient temp., hand held IRT
Chan et al. (2004)	Study the efficacy of IRT as proxy to clinical thermometers, exertion, & highest anatomical thermal yield	Three different models by FLIR: PM595, SC320C, & S60; uncooled, thermal sensitivity of .08°C @30°C, fixed IR model, adj. emissivity medical grade; spectral range – long wave; focal plane array, adj. for ambient temp., accuracy +/- 2°C, range -40-1500°	1) n=176 2) Exertion & surface temp.	1) Readings from frontal and lateral cephalic w/ mouth opened & closed at .5m and 1.5m; time per subj. not listed 2) Postexercise subjects surface temp. ~1°C higher 3) Study conducted indoors, HK hospital 4) ε=.98 5) Regression, sensitivity, specificity analysis 6) Data from SARS epidemic in Hong Kong	1) Threshold temp. 37.5°C by sen./spec. 2) Frontal view w/mouth open (r=0.45), closed (r=0.48); lateral IRT reading @ .5m compared w/ oral (R^2=0.625), frontal IRT reading @ 1.5m comp. w/ oral (R^2=0.061); sensitivity 83% & specificity 88% @ threshold of 37.5°C; lateral ceph (R^2=.56), forehead (R^2=.26)	1) Pros: optimal anatomic region screened, ack. of ambient conditions, medical grade equip., adj. for emissivity, fixed IRT 2) Cons: did not show comparison results of various cameras used; did not list screening time per subj.; 99 of subjects were healthy clinic attendees, core-2-surface adjustments not listed, SOPs not listed, calibration not listed

(*table continues)*

Reference	Objective(s)	Equipment	Sample Size/Variables affecting measurement	Methodology/ Analysis	Results	Pros / Cons
Ng DK et al. (2005)	Study the efficacy of noncontact IR readings from frontal cephalic on pediatric (1mth – 18yrs) population	Standard Instruments, ST 8812, w/laser pointer, fixed ε=0.95, temp. range of -50-500°C, audible over range, no adj. for ambient temp., industrial grade IR, no adj. for C2S	n=567	1) Readings from frontal cephalic (forehead) at 5cm for ~5s per subj. 2) Subj. temp >38°C considered febrile 3) Study conducted indoors, ambient temperatures monitored 4) ε=0.95 5) Regression, ROC, PPV, NPV analysis 6) Data from SARS epidemic Hong Kong	1) Threshold temp. 35.1°C through ROC analysis 2) Sensitivity 89.4%, specificity 24.1%, PPV 33%, NPV 98%, tympanic & IRT ranged from -0.7°C to 5.0°C, deviation (Z=1.107, p=0.172), IR showed slight lwr; r=-0.264, p<.01; ROC (AUC) = 0.868 (95% CI 0.831-0.905)	1) Pros: optimal anatomic region screened, ack. of ambient conditions, and room temp. monitored and controlled, calibration listed 2) Cons: industrial IR unit used, not medical grade, 1-9 measurements per subj., miss rep. of ROC curve, low sen./spec., PPV/NPV
Chiu et al. (2005)	Study the efficacy of IRT for selection of subj. w/SARS	Digital Infrared thermal imaging (DITI), spectrum 9000MB Medical Thermal Imaging System, adj. emissivity, adj. for ambient temp., cooled, thermal sensitivity of .08°C @30°C, 60 frames per sec., fixed IR model	1) n=993 2) False negative produced by sweating subj. & decreased sensitivity	1) Readings from frontal cephalic (forehead/medial canthus), distance and time not listed 2) ε= not listed 3) Specificity & sensitivity analysis 4) Data from SARS epidemic in Taiwan, hospital indoor setting	1) Threshold temp. 37.5°C, no listing as to why 2) Sensitivity was 75%, specificity 99.6%	1) Pros: frontal cephalic region screened; ack. of ambient conditions and room temp; calibration by black-body listed; medical grade equip. used; large sample size 2) Cons: distance from camera to subj. not listed; time of scan per subj. not listed; emissivity not mentioned, core-2-surface corrections not mentioned

(*table continues)*

Reference	Objective(s)	Equipment	Sample Size/Variables affecting measurement	Methodology/ Analysis	Results	Pros / Cons
Hausfater et al. (2008)	Study the efficacy of IR readings for recognition of febrile subjs.	Raytek Raynger MX2 Infrared Thermometer (industrial grade), no image display, adj. emissivity, no C2S adj., uncooled system, hand held model	1) n= 2026 2) Age listed as variable that interferes w/ cutaneous measures 3) Fever was listed as >38.0°C	1) Readings from frontal cephalic (forehead) distance and time not listed 2) ε= not listed 3) Study conducted indoors at a hospital in France 4) ROC, multivariate regression analysis between tympanic and infrared measurements, sensitivity and specificity, PPV, NPV	1) Threshold temp. by ROC 38.5°C 2) Sensitivity at ≥38.0 was 82%,specificity was 77%; PPV 10%, NPV 99%	1) Pros: identifying age as a potential variable for surface temp readings; indoor temp monitored; humidity was not listed 2) Cons: hand held unit so distance from subj to IR might alter, emissivity correction not listed, core-2-surface corrections cannot be made with this IR equip., equip. not capable of measuring medial canthus temp.; no calibration listed
Ring et al. (2008)	Study the thermal yield zone for IR in pediatric (1-17yo) subj. w/ fever and compare to clinical thermometry	Three different models by FLIR: 350, 620, & T400; uncooled, thermal sensitivity of .08°C @30°C, fixed IR model, adj. emissivity, medical grade; spectral range – long wave; focal plane array, adj. for ambient temp., accuracy +/- .5°C, range -40-1500°C	1) n=191 2) No association w/ age and gender in study	1) Readings from frontal cephalic (forehead/medial canthus), distance 0.5m, and time not listed; mounted on tripod, camera adjusted to height of subj., subjs were seated, target zone was focused on both eyes and then forehead measurement; small children seated on lap of parent 2) ε= not listed 3) Data from a Warshaw Hospital, Poland, indoor setting	1) Threshold temp. 37.5°C 2) Temperatures above 37.5°C should be considered febrile due to +/- 0.5°C tolerance 3) Noted, when camera is mounted above subj. erroneous temperature can result 4) Hats, sunglasses, eye glasses, surgical masks can alter IRT readings; forehead less reliable to eye region	1) Pros: frontal cephalic region screened; control of ambient conditions and room temp; calibration by black-body listed; medical grade equip. used; use of ISO standards (SOP); mentioned camera plane parallel to ground for direct facial 2) Cons: distance from camera to subj. not listed; time of scan per subj. not listed; emissivity not mentioned, core-2-surface corrections not mentioned

(*table continues)*

Reference	Objective(s)	Equipment	Sample Size/Variables affecting measurement	Methodology/ Analysis	Results	Pros / Cons
Chiang et al. (2008)	To evaluate the sensitivity & specificity of IRT, ambient discrepancy, distance between subj. & IRT	DITI/Thermoguard Medical Thermal Imaging System, adj. emissivity, adj. for ambient temp., cooled, thermal sensitivity of .08°C @30°C, 60 frames per sec., fixed IR	n= 1032	1) Readings from frontal & lateral cephalic; distance 0, 5, 10m; time not listed 2) ε= not listed 3) Study conducted indoors at a hospital in Taiwan 4) ROC, regression, ANOVA (ambient temp.), sensitivity & specificity, PPV, NPV analyses	1) Threshold temp. by ROC 36.5°C 2) Thermoguard sensitivity: 0m, 13%; 5m, 45%; 10m 57%; specificity: 95%, 70%, 85%; DITI sensitivity: 0m, 32%, 5m, 40%, 10m, 24%; specificity: 89%, 77%, 93% 3) Outdoor/indoor influence (F=4.112, p=0.002)	1) Pros: C2S corrections made; temp readings; indoor temp monitored; medical grade IRT 2) Cons: humidity not monitored, emissivity correction not listed

(*table continues*)

Reference	Objective(s)	Equipment	Sample Size/Variables affecting measurement	Methodology/ Analysis	Results	Pros / Cons
Nguyen et al. (2009)	Study the efficacy of mass screening for fever using IRT	Three different models: FLIR, OptoTherm, Wahl; all uncooled, thermal sensitivity of .08°C @30°C, fixed IR model, adj. emissivity, medical grade; spectral range – long wave; focal plane array, adj. for ambient temp., accuracy +/- .5°C, range -40-1500°C	1) n=2873 2) Self reported fever in study; sensitivity 75%; specificity 84.7%, PPV 10.1% 3) Higher IRT measurements in males	1) Readings from frontal cephalic (medial canthus), distance 10ft, 10 s per subj. 2) ε= not listed 3) Multiple intercity hospitals, approached people in ER and asked if they had a fever 4) Cross-section study, hospital chosen based on patient volume, >18 yo for participants, IRT selected by competitive bidding process and medical grade for fever detection, conducted 7 days a week, verbal and signed consent	1) Threshold temp. 38°C 2) OptoTherm/FLIR greater sensitivity (85.7% & 79.0%), specificity (91.0% & 92.0%); Opt: r=.43; FLIR: r=.42; Whl: r=.14 3) when compared to oral temp, IRT predicted temp better than self report 3) IRT could provide proxy for mass fever detection 4) ROC analysis, Opt (96.0%), FLIR (92.1%), Whl (78.8%) 5) Lower cutoff temp assure fewer false negatives	1) Pros: frontal cephalic region screened; control of ambient conditions and room temp; calibration by black-body listed; medical grade equip. used 2) Cons: distance from camera to subj. not listed; time of scan per subj. not listed; emissivity not mentioned, C2S corrections not mentioned; equipment mounted at angle from subj.

Thermal Target Zone

Validity and reliability both suffer if a thermal rich anatomical target zone is not empirically standardized, as consistent readings that closely correlate to core temperature are needed. The human body from head-to-toe emits infrared radiation with rich districts of the frontal cephalic, lateral cephalic, orbital (medial canthus), buccal, cervical, axillary, perineal, and plantar regions of the body – where arteries are superficially located near the skin surface (Marieb, 2001). However, some of these locations are excluded (e.g., axillary, perineal, and plantar) from assessment by IRT, due to clothing that could diminish or block accurate thermal readings, the inefficiency of having subjects disrobe to expose regions, and privacy issues. As a result, general anatomic regions of consideration for IRT screening include the frontal cephalic (forehead), orbital (eye region), buccal (cheek), nasal (nose), oral (mouth closed), and lateral cephalic (temple; Mercer & Ring, 2008).

Ng et al. (2004) examined the reliability of readings from general anatomic regions for IRT through quantified measures of variance analysis (coefficient of determination) within a sample of 310 subjects (see Table 2). The independent variable was core temperature assessed by aural readings from a clinical thermometer. The dependent variables were various anatomical surface temperatures as detected by the medical grade FLIR ThermaCAM S60 noncontact infrared thermal scanner. The results suggested that the most consistent readings and maximum temperature were obtained from the eye region ($R^2 = .55$), more specifically the medial canthus that is located between the eye and the nose (Ng et al., 2004). Another analysis in this study determined

that the forehead was the second region of choice for increased thermal radiance and consistent results (R^2 = .49). It is suggestive that the nearness of the ophthalmic and facial arteries and the thin mucosal epithelial of the eye region (medial canthus) provides an optimal anatomic target zone for IRT to attain the smallest correction between surface and core temperature readings (Ng et al., 2004).

Not all studies have shown the ocular region to have the highest thermal yield. Chan et al. (2004), using three similar medical grade IRT cameras (FLIR model PM595, SC320C, and S60) in a sample of 176 subjects (see Table 2), found the highest thermal yield with comparison to a clinical thermometer was at the lateral cephalic (ear) region (R^2 = .56) and frontal cephalic (R^2 = .26) regions. Furthermore, Chan and colleagues study accounted for optimal distance from camera-to-subject, ambient temperature, emissivity, exertion levels of participants, and personal protective equipment (face mask) that may cover thermal rich target zones.

The thermal target zone for consistent IRT readings is also linked to specific infrared equipment (ISO, 2008). Specifically, medical grade IRT devices have an adjustable field of view that can enable the operator to hone the camera on the facial region and the device has integrated software that directs the unit to scan for the highest thermal yield within this view. Accordingly, from chin-to-forehead and ear-to-ear (i.e., frontal cephalic region) the highest thermal reading within will be displayed, which includes the medial canthus (ISO, 2008). For this reason, medical grade IRT models prove to be superior as they are not single focusing instruments. They capture multiple split second readings across the entire facial plane, as opposed to industrial or low grade

IR models that have a single focal reading that may or may not be the most thermal rich facial region to scan (ISO, 2008; Ring et al., 2010). Superior IRT equipment is derived from ISO standards that are established from experts in the industry, technical developers, and researchers who are nationally selected to publish these technical guidelines (e.g., Ng et al., 2004; Ring et al., 2010; ISO, 2008). Thus, the determination of maximal surface temperature, as assessed by infrared systems, may be reduced when using industrial or low grade IR models as defined by ISO standards (ISO, 2008).

Not only have consistent IRT readings been linked to a particular zone, but more specifically to a precise anatomical landmark within this zone that must be observed during IRT screening. The general consensus among the IRT community suggests that the strongest association with consistent thermal emittance is located at the medial canthus of the eye (Mercer & Ring, 2008; Ng, 2005; Ng, Kaw, & Chang, 2004; Ring et al., 2010; ISO, 2008). This conclusion primarily stemmed from Ng et al.'s (2004) study that specifically researched the optimal IRT thermal target zones of the face. Ng et al.'s optimal thermal zone findings (medial canthus) were later used in other studies (e.g., Chiu et al., 2005; Nguyen et al., 2009: Ring et al., 2008) and this area was defined as the most select thermal target zone by the International Standards Organization for IRT screening (ISO, 2008). Nevertheless, environmental conditions can also influence IRT measurements.

Environmental Inferences

Environmental conditions can present as some of the most influential variables affecting reliability and validity of IRT readings (Deng & Liu, 2004). As a result, one must control these conditions to ensure the accuracy of IRT derived temperatures. The

primary adjustments to mitigate environmental variance are skin emissivity, core-to-surface temperature adjustments, and ambient temperature recognition through use of black body corrections (Ng, 2005).

Emissivity

Emissivity relates to a material's surface radiation efficiency and is a value between zero and one; shiny surfaces (e.g., silver) have values near zero (highly reflective/emit less radiation), while flat and dull surfaces (e.g., skin) have a value near one (highly absorbing/emit greater radiation; Table of Total Emissivity, 2010; Giancoli, 1998). Accordingly, human skin has an innate quality, as rated by its emissivity (ε = 0.98), to significantly radiate absorbed energy (Deng & Liu, 2004). In other words, skin has a nearly perfect emittance attribute. This attribute establishes and distinguishes the skin's identification from other objects that are in the field of view, which is critical because everything above absolute zero (-273°C/-459°F) emits infrared radiation (Giancoli, 1998). Consequently, to distinguish between other materials in the field of view, emissivity creates a semi-filtrate of environmental (i.e., air temperature, surface reflection, and objects emitting heat) conditions and may help to reduce skewed subject temperature readings (Table of Emissivity, 2010). IRTs without adjustability for emissivity (e.g., nonmedical grade IRT) lack the ability to hone in on the specific emissivity characteristic of human skin, which could attenuate reading accuracy and expedience of definitive surface temperature readings (ISO, 2008; Chan et al., 2004; Ng et al., 2004). In essence, IRT studies and technical references that addressed effects of emissivity only mentioned how it should be an input into the IRT prior to calibration; however, no study to date has tried various emissivity settings to show effects of this

alteration on temperature measurements. Nonetheless, emissivity of surface temperatures is a well studied material property that applies to infrared measurements and should be expanded into IRT research by testing various emissivities to explore the actual influences of this adjustment on surface temperature measurements (Giancoli, 1998; Togawa, 1989).

Core-to-surface Heat Transference

Radiation is energy transfer by electromagnetic waves from all objects and is proportional to temperature and surface area, and is dependent on emissivity (Giancoli, 1998). The electromagnetic waves of concern in this study are infrared, which IRT captures to approximate surface temperature (Giancoli, 1998).

Internal heat (body core temperature) is attenuated as it is released to the surface. As a result, to ensure reliability of IRT readings one must adjust for core-to-surface heat transference. Typically, the core-to-surface transference is between three to four degrees Fahrenheit (PalmerWahl Instrumentation Group [PWIG], 2009); however, the PalmerWahl IRT manufacturer suggested using ten subjects' temperatures from a clinical thermometer and correcting IRT temperature readings until it matches within +/- 1.0°F from clinical thermometer readings. Likewise, the calibration must be completed in the same environment where the IRT will be utilized to avoid ambient temperature biases (ISO, 2008; Ng et al., 2004; PalmerWahl, 2009; Ring et al., 2010). Notably, the IRT literature does not explicitly define how the researchers accounted for core-to-surface calibrations in their studies. Rather, the researchers (viz., Ng et al., 2004; Ring et al., 2010) merely addressed that this calibration was accounted during final IRT calibrations. This adjustment is specific to each medical grade IRT model and guidelines for this

adjustment are found in the manufacturer instruction manual. Additionally, the manufacturers can be contacted directly to assist with the calibration process (PWIG, 2009).

Ambient Temperature

Ambient temperature is another environmental variable that must be taken into consideration to maintain accuracy of IRT readings. Even if environmental conditions are accounted for and controlled to IRT manufacturer recommendations, calibrations are still required to permit the IRT device to thoroughly compensate between mediums (ISO, 2008). In particular, IRT is a noncontact apparatus that acquires readings from the skin (medium 1) and compensates for the air temperature between the camera and subject (medium 2). A comprehensive IRT model will have the capability to be calibrated according to room temperature (ISO, 2009; Ring et al., 2010). This calibration is accomplished by focusing the IRT on a blackbody, an object that absorbs nearly all radiation falling on it, which attunes the camera to zero-out room temperature disturbances from medium 2 that may alter readings (Fowler, 2008; ISO, 2009).

Moreover, measuring total IR of an object is acquired or delivered in several ways: emission, absorption, and reflection (Giancoli, 1998). As a result, fluctuations in ambient temperature can significantly alter subject IRT readings. For instance, a resting healthy individual typically produces heat internally at an approximate rate of 100 watts and this release is referred to as emitted heat (Giancoli, 1998). Although this emission of IR heat is reasonably constant, the blackbody-like properties of the human skin (previously discussed under the Emissivity section) can significantly facilitate increased total IR emission because good emitters are also good absorbers of infrared heat, yet

reflect IR poorly – much like human skin (Giancoli, 1998). Consequently, if subjects are in temperature extreme conditions (e.g., outside in the heat of summer or cold of winter prior to screening, or in an abnormal room temperature setting) they could potentially yield erroneous surface readings that are not indicative of actual core temperature – thus noted as convective attributes that may potentially skew IRT readings (Ng et al., 2004).

Following this further, thermal stability is another ambient temperature influence that could alter or diminish the accuracy of the IRT technology. Thermal stability primarily includes the IRT storage temperature range and equilibrium period necessary when moving the IR camera from one location to another or initial set-up after IRT has been in storage. PalmerWahl IRT manufacturer suggested storing the IR camera in temperatures close to the expected temperature range where the camera will be operated (PWIG, 2009). By doing so, optics will not be attenuated by condensation, prompt blackbody calibration can be completed, and equipment equalization is minimal (Thomas, 2007).

Finally, another ambient environmental condition to consider is humidity, as IR can be absorbed by water vapor (Giancoli, 1998). More definitively, a thermal imager is designed to function in unwavering indoor environments highlighted as an ambient temperature range of 20°C to 25°C (68°F to 77°F) and room temperature stability of +/- 1°C, with a varied relative humidity range no greater than 40% to 75% (Ng et al., 2004). Ng et al. (2004) did not discuss how or where their environment guidance was produced; however, their guidance mimics the PalmerWahl IRT manufacturer and ISO guidance (ISO, 2008; PWIG, 2009).

To summarize, environmental conditions can influence IRT measurements although many of these influences can be adequately managed. To focus on human skin, an IRT must be amendable to emissivity adjustments (ISO, 2008; Chan et al., 2004; Ng et al., 2004). Core-to-surface tunings must be made to adjust for heat transference (ISO, 2008; PWIG, 2009; Ring et al., 2010). Additionally, an IRT must be modifiable to blackbody calibrations to adjust for ambient environmental conditions that may affect IRT readings. IRTs must also be stored and operated in a similar ambient temperature conditions that lend to prompt calibrations and accurate IRT temperature measurements (PWIG, 2009; Ng et al., 2004; Thomas, 2007). Although little research on these parameters exists, the general procedure is for IRT users to reference their equipment manufacturer guidelines and the IRT International Standards Organization specifications (ISO, 2008). While these adjustments and modifications can contribute to the accuracy of IRT temperature measurements, infrared impeding materials must also be discussed as they can affect IRT measurements as well.

Infrared Impeding Materials

Infrared impeding materials are of significance due to the fact that they may reduce the accuracy of IRT readings. Long-wavelength infrared, a band of radiation between eight and 15 micrometers (μm), is the region that noncooled IRT cameras utilize to gather a passive image from thermal emissions (Giancoli, 1998). Within this band, certain materials used on a daily basis could attenuate the IR signature captured by IRT. Polycarbonate and polysulfone materials, used ubiquitously for their durability and stability at high temperatures, can significantly attenuate infrared (Bendiganavale & Malshe, 2008). The most common objects using these materials are found in eyeglasses

and if worn during IRT screening would cover the medial canthus, which is one of the most thermal rich target regions as previously described (Cheung et al., 2008; ISO, 2008; Ng et al., 2004). Infrared reflective inorganic pigments used in clothing may also attenuate the subject's IR signature when screening with IRT (Bendiganavale & Malshe, 2008). No study has specifically studied the effects of eyeglasses or any other IR impeding materials on IRT measurements, as the IRT visualization (picture) clearly shows a void of heat (black spot) from anything attenuating IR emittance and the impeding material is simply removed during the process.

Facial cosmetics have also been considered as impeding materials. However, Cheung et al. (2008) found only minor changes on facial surface temperature from the use of foundation, powder, and lotion. Specifically, this study was conducted in a controlled setting using three women (age 20-30) who were randomly selected to participate. These subjects were asked to apply lotion, foundation, and powder in sequence to the targeted zone (frontal cephalic). IRT measurements were then taken before and after each of the applications. The final results concluded that foundation had the most attenuation of IRT readings (+/- 0.6°C), and powder and lotion had the same attenuation (+/- 0.1°C; Cheung et al., 2008). Even though these results are minimal, they support the practice that when an individual is bordering a febrile surface temperature (e.g., 37.5°C/99.5°F) they must be subjected to a secondary oral temperature screening to ensure the absence of fever that might be masked by facial cosmetics or other covariates previously discussed.

Discussion of Methods for Research on the Use of IRT in Syndromic Surveillance

IRT is a modern technology that may be used in public health for mass screening of febrile illnesses and holds promise as a syndromic surveillance tool. However, the current literature only provides information as to the efficacy of IRT with comparison to clinical thermometers. More specifically, several studies (e.g., Chiu et al., 2005; Ng, Kaw, & Chang, 2004; Ng, 2005) have made the association that IRT is an effective instrument for identifying febrile individuals, which in turn has been the cardinal sign of some severe acute respiratory infections (Ksiazek et al., 2003). In essence, these studies clearly defined IRT as an effective alternate to clinical thermometers when assessing temperatures in a mass screening environment. Many factors, as previously discussed, may cause elevated surface temperature and are not necessarily a result of an infectious disease; consequently, diagnostic measures must also be used with IRT captured cases (individuals with elevated surface temperature). Additionally, to ensure consistent, reliable, and accurate IRT measurements, standardized methods and control of variables must exist. An overview of the most relevant IRT-febrile illness studies serves to illustrate and guide how all of these factors are accounted for in research studies in this field.

Ng et al.'s (2004) study design used a cross-sectional sample from a hospital setting in Singapore during the SARS epidemic of 2003. Ng et al.'s objectives were to investigate the optimal thermal region for screening with IRT and the ideal threshold temperature. As such, the study utilized a long-wave IRT camera (medical grade), a sample of 310 individuals from the emergency room, and screened all subjects in an indoor environmentally controlled area. Additionally, the study accounted for emissivity,

ambient temperature conditions (e.g., humidity and room temperature), distance from IRT to subject, length of time each subject was screened, anatomic region screened, and compared this data through specificity, sensitivity, ROC, and regression analyses. Ng et al. (2004) identified the optimal thermal target zone in their research by screening various areas of the face and comparing them to oral temperatures. Using regression analysis the medial canthus was recognized as the optimal thermal target zone, as listed in Table 2. Furthermore, Ng et al. identified their optimal threshold limit through sensitivity and specificity comparison by ROC analysis. This threshold (specific to their study) would be the maximal temperature that differentiated between febrile and afebrile subjects. Additionally, Ng et al. referenced emissivity tables to document the specific emissivity of skin and how IRT equipment must use ($\varepsilon = 0.98$) as this quantity distinctively relates to human skin (Deng & Liu, 2004). Finally, Ng et al. (2004) emphasized the importance of screening only one subject at a time to ensure proper focus of the IRT camera, distance, and time of individual screening. As a result, this study identified the optimal thermal target zone, recognized the importance of single subject stationary screening and consistent distance between subject and IRT (in accordance with manufacturer guidelines), and mentioned the need for monitoring and controlling environmental conditions that may influence IRT measurements. This study also referenced the human skin emissivity parameters for IRT calibrations.

Chan et al. (2004) completed a cross-sectional study using hospital participants during the Hong Kong SARS epidemic of 2003. The objectives of this study were to examine the efficacy of IRT as a proxy to clinical thermometers and the effects of exertion on IRT measurements. This study utilized a long wave IRT camera (medical-

grade) and a sample size of 176 subjects. Additionally, Chan et al. accounted for emissivity ($\varepsilon = 0.98$), ambient conditions monitored, distance from IRT to subject were recorded, and data was compared using sensitivity, specificity, and regression analysis. Furthermore, Chan et al. (2004) identified the affects of exertion on IRT measurements by taking a pre and postexercise (five minutes of vigorous soccer) IRT and aural temperature readings of 15 individuals. Their results suggested exertion did have an effect on IRT measurements by increasing the surface temperature approximately one degree Celsius ($p < 0.05$) higher than preexercise measurements (Chan et al., 2004) and thus supports how exertion could cause elevated surface temperatures that are not indicative of febrile illness. In addition, this study reiterates the use of emissivity calibrations ($\varepsilon = 0.98$) and that IRT surface temperature readings can serve as a proxy to aural temperature measurements based off of sensitivity, specificity, and regression comparisons (Chan et al., 2004).

Ring et al. (2008) executed a cross-sectional study with participants from a hospital in Poland. In this study, Ring et al.'s objectives were to investigate IRTs ability to function as a proxy to clinical thermometers. This study utilized a long-wave IRT camera (medical grade), a sample of 191 subjects, and screened all participants in an environmentally controlled room of the hospital. Moreover, Ring et al. accounted for emissivity ($\varepsilon = 0.98$), black-body IRT calibrations, utilized the medial canthus target zone, proper adjustment of IRT camera to subject height, and mentioned guidance from the ISO for establishing an IRT screening station. This study was the first to address the ISO reference guidance for screening human subjects with IRT. Above all, the ISO guide has established the methods for selecting the appropriate IRT equipment, calibrations that

must be completed, materials that can attenuate infrared readings, optimal thermal target zone, and environmental considerations that can attenuate IRT measurement (ISO, 2008). As such, the methods in this study form the basis from which further research must follow in order to maintain continuity within the IRT research field.

Summary and Transition

Studies of IRT emphasize its ability to function as a proxy to clinical thermometers under the auspices of certain limitations and with use of select anatomical regions. In addition, these studies draw attention to its sensitivity and specificity to achieve reliable surface temperatures that correlate to core temperature. However, some studies with differing conclusions exist within the IRT literature (e.g., Cheung et al., 2008; Chiu et al., 2005; Hausfater et al., 2008). Particularly, these discrepancies existed as a result of methodological differences: disregard for the need to use medical grade IRT equipment, ambient temperature that was not controlled when operating IRT, ambient temperature that was not accounted for by use of a black body, emissivity that was not accounted for in readings, core-to-surface corrections that were not utilized, or the fact that only single region scanning was performed – all of which could have contributed to the reduced sensitivity or specificity seen in those studies. Ng et al. (2004) and Chan et al.'s (2004) research were the first studies to address and account for medical grade IRT equipment, ambient temperature influences, and proper prescreening calibrations in their research. Several recent studies have also followed suit (Chiang et al., 2008, Ring et al., 2008, Nguyen et al., 2009) and used the recent guidance of the International Organization for Standardization technical reference for IRT (ISO, 2008). With the exception of these studies and the technical reference, IRT research has lacked consistency with the

equipment used, control of covariates affecting measurements, and standardized protocols for utilizing this equipment that may have led to the altering results throughout the literature.

Given these inconsistencies the question remains, does IRT have the ability to identify subjects with ILI based on their thermal signature? The literature indicates IRTs ability to approximate surface temperature with comparison to clinical thermometers, yet no study to date has been completed to examine the efficacy of IRT (a screening tool) with diagnostic ILI confirmation of those subjects identified by IRT as having an elevated surface temperature.

Chapter 3 will outline the cross-sectional study design that was chosen for this exploration. In addition, it will explain in detail the specifics for the research design and approach, justification for this approach, selection criteria for setting and sample, instrumentation, and data analysis. Most importantly, chapter 3 offers the fundamental construction of the components for correlated associations between IRT temperature measurements, gender, and ILI.

Chapter 3: Research Methods

Introduction

This chapter will document the quantitative methodology utilized to investigate the efficacy of fixed infrared thermography (IRT) for the identification of subjects with influenza-like illness (ILI) based on elevated surface temperatures. Included in this discussion are the problem statement and research design and approach that explain the rationale for utilizing a retrospective cross-sectional study design. There will also be a discussion of the setting and sample that includes a description of the military population used in this study, inclusion and exclusion criteria for participants, and the justification for the sample size selected for this study. Lastly, an in-depth explanation of the analyses used to determine IRT efficacy and gender-specific correlations between IRT surface temperatures and oral temperatures will be provided along with the details for the protection of participants' rights.

Research Design and Approach

This study used an archived dataset of participants from the U.S. Navy and Marine Corps that were afloat in the Pacific Ocean whose vessels had been identified through the PHAS. The PHAS system identifies U.S. Naval vessels with crew members who have exceeded a disease and non-battle injury prevalence rate of 300 per 1,000 persons each month. If these alerts document an exceeded shipboard endemic disease threshold, then military public health teams may be deployed to the alerted ship's location for a follow-up investigation. This current study used retrospective data by such a public health team. The linkage with the emergency public health investigational team was critical for providing the IRT surface temperatures, oral temperatures, environmental

ambient conditions, health questionnaire data, and laboratory diagnostics used for IRT efficacy determination. As such, a retrospective cross-sectional design was the most fitting approach for this study for practical reasons.

The shipboard outbreak conditions provided an ample amount of febrile individuals to support the predetermined sample size (explained below). To establish the efficacy of IRT for the identification of subjects with ILI in this study, however, the confirmation or absence of ILI needed to be diagnostically determined. Therefore, all participants were screened by IRT and compared to nasopharyngeal, oropharyngeal, and serological diagnostic confirmatory results for ILI from the public health team's investigation. The collated results facilitated the determination of true positives, true negatives, false positives, and false negatives that were used in ROC analysis to determine IRT efficacy (see Figure 4).

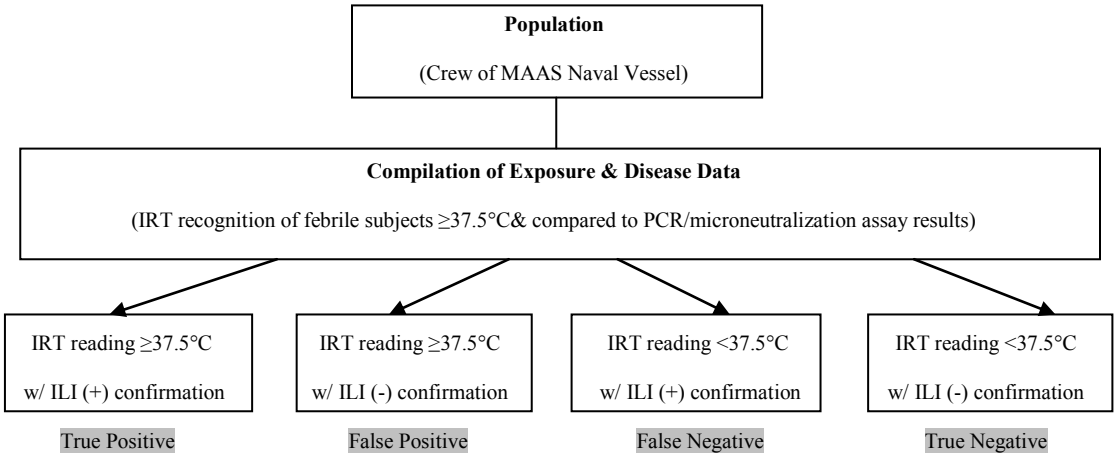

Figure 4. IRT cross-sectional design.

Consequently, data for this research were derived from archival IRT surface temperatures, oral temperatures, environmental ambient conditions, health questionnaire data, and laboratory diagnostics on all participants of the selected multipurpose amphibious assault ship (MAAS). The details of the IRT measurements and public health outbreak study results will be further explained in the next section.

Setting and Sample

The research archived data population for this study was recruited from Sailors and Marines that were aboard a MAAS during an ILI shipboard epidemic in the Pacific Ocean. This class of vessel was selected due to these ships' large (male and female) crew of approximately 1,500 Sailors and Marines, ample medical staff, and laboratory supportive capabilities (i.e., PCR to determine if crew members reporting to sick call actually have influenza). Notably, all MAAS participants were utilized in the public health study, not only those who reported to sick call. Study recruitment from the public health team took place, in part, by conducting an information brief over the ship's intercom (immediately upon the public health team boarding the ship), which emphasized the voluntary nature of their study, purpose of this research, information about the IRT technology, safety of the screening device, location of IRT screening on the ship, and hours of operation. Flyers describing the study were also distributed shipwide.

Participants had to meet the following criteria to be included in the public health study: (a) be part of the ship's crew completing the sea deployment in San Diego, as some crew exited in Hawaii and, as a result, did not have serology/PCR results; (b) have no fixed materials that could be blocking the face or neck (viz., bandages, eye patches, or other medical nonremovable materials) of the participant; (c) be ambulatory so that they

could be screened with the IRT equipment; and, (d) could not be in the ship's intensive care unit or in any other impaired health state where participation in the study would include possible interruption of essential therapeutic care. While the entry criteria of the sample are significant, the setting for the public health team shipboard investigation used for this study through an archival data set is equally important.

In the event of a shipboard outbreak, the PHAS will send out a notice that a MAAS has exceeded the threshold limit of ILI cases among its crew. This notice alerted authorities in the Pacific Fleet who determined if a public health investigation was warranted. Upon receipt of that information, coordination was made with the Harbor Master to determine when the ship would arrive at the port in Pearl Harbor, Hawaii.

On the day of the ship's arrival, all crew members were required (mandated by state port authorities) to have their oral temperatures taken prior to liberty leave to ensure they were afebrile. This screening process was conducted by the ship's medics at one central location aboard the MAAS and offered from 0700 until 2200 on the first day of arrival into Pearl Harbor. At that location, crew members were also verbally informed by the public health team about the study and asked if they would participate in the public health research. Crew members were given an IRT information/data sheet and consent form, and any questions they had were answered prior to entering the IRT station. Individuals who declined participation in the study were noted as "NO GO" on their consent form and directed to the oral temperature reading station (skipping the IRT station; see Figure 5). Crew members who agreed to participate in the IRT study were asked three questions (if they feel/felt feverish, had taken any fever reducing medication(s), or had a current flu shot), had their IRT surface temperature recorded

(environmental conditions were also noted), and oral temperatures taken by ship medical staff and public health team. The public health team IRT station was established in near proximity to the oral thermometry process conducted by the onboard medics. The near proximity ensured minimal participant uncertainty as to the process, as well as the collection of the data sheets prior to participants leaving the ship.

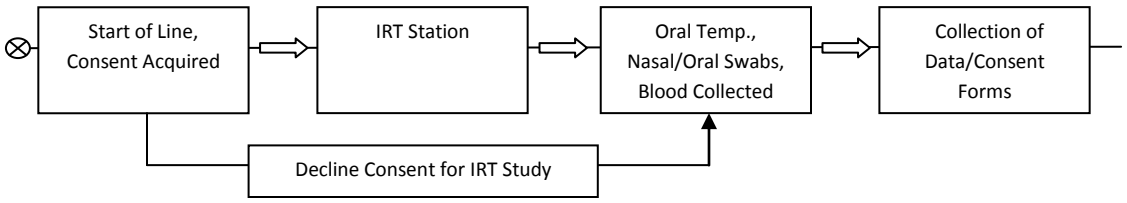

Figure 5. IRT station with inclusion of emergency public health investigation.

Approximately two weeks after the initiation of the public health team study described above, the archived dataset was made available for analysis in this research. In preparation, permission had been acquired (see Appendix C) from the armed forces health surveillance center (AFHSC) to receive archived data from the public health team study to include: participants age, sex, ship ID tag number, current fever status, antipyretic intake, flu vaccination status, air turbidity, room temperature, humidity, IRT operator (individual from public health team), serologic/PCR results, IRT temperature, and oral temperature. Additionally, the ship name, date of emergency outbreak investigation, and deployment cycle was used to ensure this study was properly matched to correct public health team archived dataset. Results were obtained via encrypted and password protected email from AFHSC and in a password protected spreadsheet format.

For the laboratory diagnostics, two procedures (nasopharyngeal swabs for PCR and blood draws for serology) were attempted to be completed by the public health team on all participating crew members; however, due to the discomfort of the nasopharyngeal and oropharyngeal swabs, participants may have only elected for the blood draw. If no diagnostic procedures were completed due to the inability to draw samples (e.g., dehydration, collapsed vein, extreme discomfort), "NO SAMPLE" was listed under the participant's ship ID tag number, and that participant was not included in this IRT study due to the lack of ILI confirmation. Notably, swab cultures were conducted immediately after IRT screening, although blood draw did not occur until 10 days after the IRT screening to allow sufficient time for seroconversion of the exposed individuals (i.e., individuals with fever). In general, seroconversion can take 7 to 14 days to mount the development of detectable antibodies that are later identified through a microneutralizaton assay procedure (Flint, Enquist, Racaniello, & Skalka, 2004, p. 579; Murphy, Gibbs, Horzinek, & Studdert, 1999, p. 217; Sompayrac, 2002). Nonetheless, Figure 6 shows how the final results were interpreted for this study.

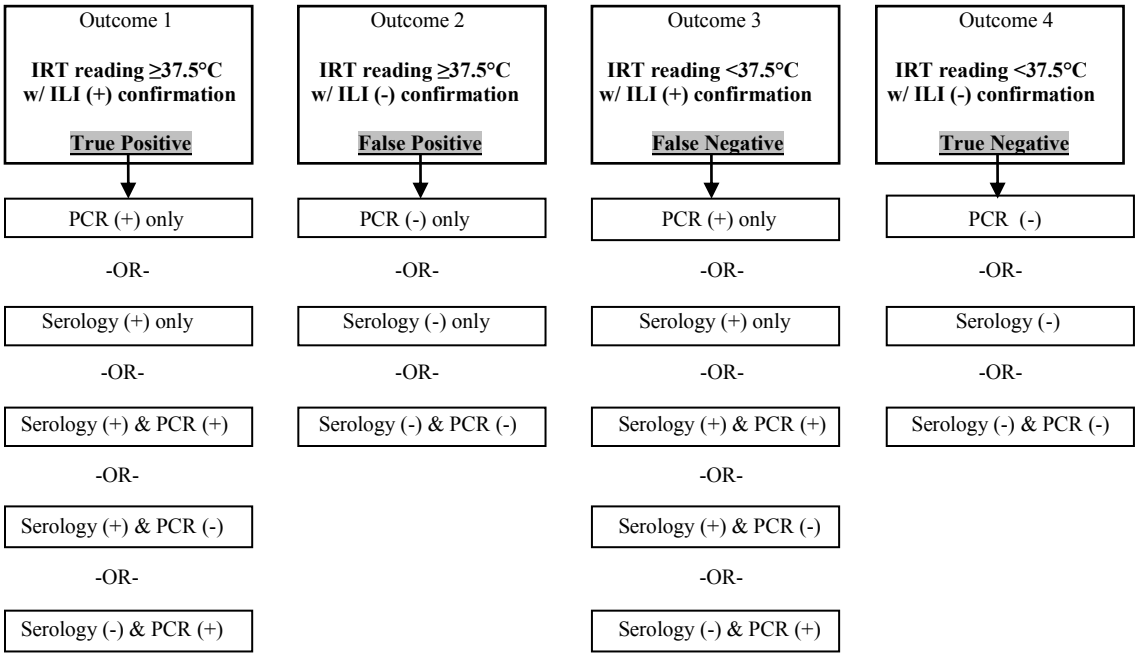

Figure 6. Example of diagnostic and IRT outcomes.

Sample Size

An *a priori* sample size was determined using *G*Power* (version 3.0.10) statistical software and was calculated using a point-biserial correlation as the test statistic (Buchner et al., 1997). Additionally, input parameters were set at two-tails, alpha was set at 0.05, and a medium effect size was used (r= 0.44). The effect size average was taken from the correlation coefficient (r) or calculated using the coefficient of determination (r^2) in all IRT studies that accounted for variance or used linear regression analysis to show the relationship between IRT surface temperature and the prediction of elevated core temperature. As mentioned in chapter 2, Chan et al.'s (2004) research concluded with an IRT frontal view of r = 0.54; Liu et al.'s (2004) research found an IRT frontal view of r = .25; Ng et al.'s (2004) research showed an IRT frontal view of r =

0.74; Ng et al.'s (2005) research concluded with an IRT frontal view of $r = 0.26$, and; Nguyen et al.'s (2009) research determined an IRT frontal view of $r = 0.43$ (see Table 2). These studies produced an average sensitivity of 85% and specificity of 79%, which was used in favor of IRT efficacy for recognition of febrile subjects and coupled with the findings that fever is the cardinal sign of ILI (previously explained in chapter 2). It can be assumed this effect size can be extrapolated to fit this study (CDC, 2010c; CDC, 2010i; Chan et al., 2004; Ksiazek et al., 2003; Liu et al., 2004; Ng et al., 2004; Ng, 2005; Nguyen et al., 2009). Furthermore, the statistical power standard was placed at 90% (1-ß error probability [0.90]). Given the previous parameters and estimates computed using 44 degrees of freedom, 46 subjects were determined to detect the effect size of $r = 0.44$ (see Table 3). However, the exposure (febrile disease) must be within this population. Accordingly, with an estimated shipboard outbreak prevalence of 300 per 1,000 persons each month (identified by PHAS and interpreted as a prevalence of 30%), a sample size of approximately 153 participants was needed for this study (see Table 3).

Table 3

Determination of Sample Size (Calculated by G Power Analysis, version 3.0.10)*

t tests – Correlation		
Analysis: A priori (actual population): sample size		
Input	Tail (s)	= two
	Effect Size (r)	= 0.44
	αerr prob	= 0.05
	Power (1-ß err prob)	= 0.90
Output	Df	= 44
	Sample Size	= 46
	Actual Power	= 0.9015
	Total sample size (x)	
	$x = \frac{46\ (\text{sample size})}{.3\ (\text{prevalence})}$	= 153

Instrumentation and Materials

The instrumentation used by the public health team in this study was the Palmer Wahl, HSI 2000S Fever Alert Imaging Infrared Thermography System that utilizes a long wavelength infrared emittance to determine surface temperature. According to the manufacturer (see Appendix A), the Palmer Wahl IRT can obtain a valid surface temperature in under 0.5 seconds. This IRT also includes: a calibration blackbody, core-to-surface temperature calibration, a validated surface temperature accuracy of +/- 1.0°F (~ .5°C) with comparison to an oral thermometry, a thermal image display, multiple thermal reading capability, and had adjustable emissivity (Palmer Wahl, 2009). Additionally, the selected IRT was a fixed (tripod mounted) unit that adhered to the International Standards Organization for IRT equipment and the equipment was selected

through a competitive bidding process of IRTs that met ISO standards (ISO, 2008). The HSI 2000S IRT was selected due to the lowest bid cost per unit (four IRT cameras were purchased). Additionally, the Kestrel 4500, a professional grade thermometer, was used to measure humidity, wind turbidity, and room temperature in the public health team study (see Appendix B; Kestrel Meters, 2010). Similar thermometry equipment had been used in other IRT studies to detect and monitor environmental conditions that could have skewed IRT readings (Liu et al., 2004; Ng et al., 2004; Ng, 2005; Nguyen et al., 2009). Finally, for random selection of individuals for IRT core-to-surface calibrations, a number generator was used from RANDOM.ORG (see Data Collection section).

With regard to materials acquired for this study, the public health team outbreak investigation generated diagnostic disease confirmatory results and IRT screening results that were used to determine true positives, false positives, true negatives, and false negatives for this study (see Table 6). The public health team investigation conducted nasopharyngeal and oropharyngeal swabs on all participating crew members using Dacron tip swabs inserted into the oropharynx and nasopharynx (see Appendix E) and then placed in 1- 3 mL of viral transport medium (stored at -70°C or colder, containing a protein stabilizer, antibiotics, buffer solution, and labeled with participant ship ID tag number) for later processing by the Naval Health Research Center (NHRC) in San Diego, California (CDC, 2009n). The processing used real-time RT-PCR. That assay was used to detect Influenza virus being shed by the participant (e.g., influenza B viruses, seasonal influenza A H1 viruses, seasonal influenza A H3 viruses, or the 2009 novel influenza a H1 virus). Samples were then tested using a RT-PCR detection panel developed by the

CDC, as well as an in-house assay used to detect seasonal influenza H1 and H3 strains (CDC, 2009l; Flint et al., 2004).

Approximately 10 days after the swabs had been taken (previously explained under the Setting and Sample section), blood draw was conducted on the same participants using a disinfected, peripheral venous site (approximately 5.0 mL of whole blood was collected and stored at -70°C or colder) and later processed at NHRC. The processing of those samples was performed using a microneutralization assay, which was used to detect antibodies in the blood that were against a specific virus. Those antibodies expressed if a person had been exposed to the virus, reported as seroconversion (CDC, 2009l; Flint et al., 2004). To perform that assay, NHRC used cells from an immortal cell line such as HeLa (derived from human epithelial cervical cancer cells) and grown in a 96-well cell culture plate. Then, serum that had been collected from each participant was mixed with virus. If the participant had already been exposed to the particular virus, via infection, then the serum would contain antibodies against that virus (Flint et al., 2004). While the instrumentation and materials are of significant importance to this study, the data collection conducted is of equal importance and will be explained in the next section.

Data Collection

IRT Standard Operating Procedures

As discussed in chapter 2, strict adherence to the IRT manufacturer guidelines and IRT International Standard Organization requirements for safety and essential performance of these screening devices must be sequentially followed to avoid instrumentation errors that may pose threats to internal validity. As a result, the

procedures from the public health study were gathered from the PalmerWahl® IRT manufacturer and ISO guidelines for the use of IRT devices for screening febrile individuals (ISO, 2008; PWIG, 2009). The following standardized operating procedures were conducted on all participants by the public health team:

1. Participants were verbally informed about the IRT equipment in groups of ten, provided an IRT information/data sheet/Consent form, and informed about the purpose of the public health team study and the safety of the screening procedure prior to entering the IRT station. If a participant declined to participate, their data sheet was marked ―NO GO" and they proceeded to the oral temperature and nasopharyngeal/oropharyngeal swab and blood draw station, see Figure 5).
2. Participants were asked three questions from the data sheet: (a) Do you feel like you have a fever now, or have you felt like you had a fever in the last 24 hours?; (b) In the past eight hours have you taken any medicine for pain or fever?; (c) Did you have the annual flu shot/nasal mist?
3. Participants were asked to remove hats, pull back hair from face, remove eye glasses, and other materials that may block or impede their infrared emittance.
4. Participants were asked to sit in a prepositioned chair that was 4 feet (in accordance with manufacturer guidelines) from the IRT camera.
5. Each participant was screened for a minimum of 5 seconds by IRT.
6. Only one participant at a time was screened by IRT.
7. After IRT measurements were recorded the humidity, room temperature, and wind turbidity was documented on each participant's data sheet.

8. The ship's medical staff conducted an oral temperature on every participant immediately after IRT screening and this information was recorded on the participants' data sheets (see Figure 5).
9. After all measurements had been recorded the participants were asked if he/she had any questions about the screening process.
10. Data sheets were collected at the final station by the ship's medical staff (see Figure 5).

The following items represent the IRT equipment standardizations for the public health team study:

1. IRT was stored at room temperature to avoid the needed system acclimatization prior to use (ISO, 2008).
2. IRT optic was checked for lens contamination (e.g., dust, debris, finger prints, etc.).
3. Black body calibrations were measured five times prior to IRT screening in accordance with ISO standardizations (ISO, 2008).
4. Core-to-surface adjustments were conducted at the start of the shift and taken by ten random afebrile individuals' IRT temperatures with comparison to their clinical oral thermometer readings. The differences between measurements were entered into the IRT – this method was in accordance with the manufacturer's guidance. The process for randomly selected afebrile individuals was conducted using a number generator; it was set to generate ten random integers, and valued between 1 and 20. Generated numbers were used to select afebrile individuals from the first 20 people in the line prior to

screening (if the line is larger than 20 people, the valued range was set accordingly to match the line amount of individuals). Selected individuals were asked the previously explained study inclusion information (e.g., willing to participate, signing of consent form, etc.). If an individual was to decline, another random number would be selected from the generator and the corresponding individual was selected. If a febrile individual was selected during the calibration process, they would be isolated from the group. When the IRT was calibrated, they were the first individual(s) to be screened by IRT. Individuals selected for IRT calibration were enrolled as participants in this study.

5. The screening station was conducted indoors, ambient temperature were controlled between 20°C - 24°C (68°F – 75.2°F), and with an accompanied temperature stability of +/- 1°C. The relative humidity range was between 10% - 75% and wind turbidity was monitored to ensure it was undetectable (i.e., IRT station was not set-up near an entrance/exit, A/C forced air duct, fan, etc., which may generate wind turbidity; ISO, 2008; Ng et al., 2004).
6. The wall behind the participant screening zone was previously scanned with the IRT to see if thermal emittance was detectable (e.g., hot water pipes in wall, electric circuitry, etc.), which could alter participants' readings (ISO, 2008).
7. Emissivity was set for ε=0.98 (ISO, 2008; Ng et al., 2004; Ng, 2005).
8. Threshold temperature was set for 37.5°C (Ring et al., 2008).

9. The location of the IRT station was free of environmental infrared sources such as sunlight, direct incandescent, halogen, quartz tungsten halogen, and other types of lamps that may produce significant IR signatures (ISO, 2008).
10. Area chosen for screening had a non-reflective background (i.e., cloth sheet; ISO, 2008).
11. IRT images were configured to show participants' faces, date/time group, participants' temperatures, and threshold temperature (ISO, 2008).
12. IRT targeted zone were centered on the medial canthus (eye region; Chiu et al., 2005; ISO, 2008; Ng et al., 2005, Ring et al., 2008).
13. IRT camera was mounted (fixed) and directly in front of subject (on a horizontal plane with subjects face), IRT camera at no time was at an angle while taking a thermal image (ISO, 2008; Ring et al., 2008).

Data Analyses

Two analytical methods were used to test the hypotheses in this study. The first was accomplished using receiver operating characteristics (ROC), by studying the area under the curve (AUC) of a ROC plot, which is equivalent to the Wilcoxon test of ranks and closely related to the Gini coefficient (Hanley and McNeil, 1982). This analysis assessed the ability of IRT to differentiate between febrile (with ILI) and afebrile (without ILI) participants by comparing the true positive rate versus the false positive rate (see Figure 7). ROC outputs were interpreted as: (a) excellent differentiation (0.90 - 1.0), (b) good differentiation (0.80 - 0.89), (c) moderate differentiation (0.70 - 0.79), (d) poor differentiation (0.60 - 0.69), and (e) failed differentiation (0.50 - 0.59) to show efficacy of

this screening tool (Hanley & McNeil, 1982; Swets, Dawes & Monahan, 2000). Second, a *Pearson's correlation coefficient* (*r*) test was used to measure the degree of a linear relationship between oral temperature (male/female) and surface temperature (from IRT). This unit-free output resulted in a number between -1 and +1 that revealed the degree to which the two variables are related (Brase&Brase, 1999). The two produced correlation coefficients (male and female) was then tested using a *z*-statistic, which was associated with a *p*-value, to determine if these gender outputs statistically differed from each other (a test of significant difference between correlations).

$$True\ Positive\ Rate = \frac{\text{True Positives}}{\text{True Positives} + \text{False Negatives}}$$

&

$$False\ Positive\ Rate = \frac{\text{False Positives}}{\text{False Positives} + \text{True Negatives}}$$

Figure 7. Example of TPR and FPR used for ROC analysis.

Data Analysis for Research Question 1

Can IRT, in a mass screening shipboard environment, statistically differentiate between afebrile participants without ILI exposure and febrile participants with ILI exposure? A ROC test was used (true positive rate vs. false positive rate) to quantify this research question. By studying the AUC of a ROC plot, one can assess the ability of a screening tool to discriminate between febrile and afebrile participants. ROC outputs were interpreted as: (a) excellent (0.90 - 1.0), (b) good (0.80 - 0.89), (c) fair (0.70 - 0.79),

(d) poor (0.60 - 0.69), and (e) fail (0.50 - 0.59; Hanley & McNeil, 1982; Swets, Dawes & Monahan, 2000).

Data Analysis for Research Question 2

Does the relationship between oral and IRT surface temperatures vary by gender? A *Pearson's correlation coefficient* (*r*) test was used to measure the degree of a linear relationship between oral temperature (male/female) and IRT surface temperature (male/female). This unit-free output resulted in a number between -1 and +1 that revealed the degree to which the two variables (oral temperature and IRT surface temperature) were related, as both were calculated by gender (Brase & Brase, 1999). The two produced correlation coefficients (male and female) were then tested using a *z*-statistic, which was associated with a *p*-value, to determine if these gender outputs statistically differed from each other (a test of significant difference between correlations).

Protection of Participants' Rights and Summary

In accordance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA), all personal identifiers were de-identified intrinsically as the ship ID tag numbers were cleared at the end of the deployment (approximately a week after this study), which aided participant protection in this study. The participants' ship ID tag (a number specific to that individual and used only for credit purchases while they are aboard the ship) was used as a study identifier because this number is not sensitive in nature (i.e., shipmates do not recognize each other from these numbers, Sailors are never publicly identified by these numbers, and are issued new ID tags when assigned to another ship). The only system that can couple the name with the ship ID tag number

was the onboard finance registry system that was cleared upon culmination of the deployment. Moreover, statutory conditions established by HIPAA were followed with particular emphasis towards: who was covered, disclosure avoidance, individual rights, Hawaii and California state laws, and reproduction of research materials. This study was reviewed and approved by the Walden University Institution Review Board (see Appendix F) and a Data Use Agreement was signed with the Armed Forces Health Surveillance Center (see Appendix C). Additionally, National Institute of Health (NIH), Human Research Protection training was completed by the researcher. Data integrity was maintained through password protected and encrypted email files of the archived dataset information and was stored on only one password protected internal hard drive. Hard copy datasets were shredded and electronic files will be held under password protection for five years after the completion of this research. Participants in the public health team (source of the archived dataset) study were not compensated. Individuals that meet the inclusion criteria (mentioned under the Setting and Sample section) were identified as having a signed consent form in their hands and a clear data sheet without the term "NO GO" written on the front; IRT excluded individuals (mentioned under the Setting and Sample section) did not have a signed consent form in their hands and "NO GO" appeared on their data sheet.

Moreover, due to the military population that was used in the public health team study, a voluntary public health research study could potentially be misunderstood as a directed order to participate. To avoid that misunderstanding the public health team, upon first boarding the ship, made an informative announcement over the ship's intercom that explicitly stated the voluntary nature of the study, met with the ship's senior crew

and supervisory staff to explain the voluntary nature of the study, and verbally and in writing informed all crew of the voluntary nature of the study prior to conducting the IRT research.

In summary, this chapter listed the research design and approach, setting and sample, instrumentation and materials, data collection and analyses, and efforts made to protect participants' rights. The following chapter, chapter 4, will present the results of this research.

Chapter 4: Results

Introduction

This chapter describes the analyses conducted to address this study's research questions. The participant demographics and descriptive statistics will be presented first, followed by details of the methods used to address each of the questions, including the use of ROC and linear regression analyses to statistically explain IRTs efficacy for identification of subjects with ILI. This chapter will conclude with an overall summary of results.

The data used to formulate the results below were collected from an archived dataset that was gathered by a military public health team that utilized IRT screening, oral thermometry comparison, and serological and viral specimen diagnostics to investigate an outbreak aboard a naval ship during the 2010-2011 northern hemisphere flu season. Notably, the procedures, equipment, and IRT standard operating procedures, as defined in chapter 3, were followed by the public health team to ensure accurate and reliable IRT measurements. There were no deviations from the planned protocol.

Participant Demographics and Descriptive Statistics

Participants in this study were obtained from an archived dataset that included a total of 320 Sailors and Marines that were aboard a multipurpose amphibious assault ship (MAAS) during the 2010-2011 northern hemisphere influenza season. The participant sample was comprised of 94 females (29.4%) and 226 males (70.6%). Participants ranged in age from 19 to 50 years with an average age of 22 years. The majority of the participants were European American (55.3%; see Table 4). The total MAAS crew was 603 individuals, and of that population 384 responded to this voluntary public health

study; however, 64 declined to complete the entire study primarily due to the invasive nasopharyngeal/oropharengeal swabs and blood draw diagnostic procedures. Additionally, declining individuals explicitly stated refusal to release their demographic information, prohibiting a descriptive comparison between those who completed the study and those who did not.

Table 4

Sample Demographics

Sample Size (N=320)					
Age	Range	19-50			
	Mean	22	(*SD* = 1.42)		
	Mode	20			
Gender	Male	226	70.60%		
	Female	94	29.40%		
Race	African Descent			58	18.10%
	American Indian/Alaskan Native			10	3.10%
	Asian			26	8.10%
	European American			177	55.30%
	Native Hawaiian			4	1.30%
	*Other			45	14.10%
*If participant could fit multiple categories they were instructed to choose other				N=320	

Data Screening

A complete frequency analysis was run in SPSS on all categorical data to look for outliers and possible erroneous data entries. In addition, continuous data were observed for range and summary measures beyond the mean to identify possible outliers, erroneous data and to provide study sample descriptive statistics (see Table 5).

Table 5

Descriptive Statistics of Variables

	Mean	*SD*	Median	Mode	Δ Range	Min.	Max.
IRT Surface Temperatures (°F)	98.21	1.14	98.00	97.81	7.60	95.60	103.20
Female IRT Surface Temperatures (°F)	98.24	1.07	98.20	99.50	4.90	95.90	100.80
Male IRT Surface Temperatures (°F)	98.19	1.17	98.00	97.80	7.60	95.60	103.20
Oral Thermometry Temperatures (°F)	98.39	1.21	98.20	98.90	6.50	96.00	102.50
Female Oral Thermometry Temperatures (°F)	98.29	1.19	98.10	97.90	5.90	96.00	101.90
Male Oral Thermometry Temperatures (°F)	98.43	1.23	98.30	98.90	6.40	96.10	102.50
Room Temperature (°F)	71.93	0.75	72.00	72.00	2.00	71.00	73.00
Room Humidity (%)	52.44	0.59	52.00	53.00	2.00	51.00	53.00
Wind Turbidity (non-measurable)	0.00	0.00	0.00	0.00	0.00	0.00	0.00

As shown in Table 5, the IRT and oral temperature means were very comparable with only a 0.18°F separation, which is acceptable due to the IRT inaccuracy of +/- 1°F, explained in chapter 2. Male maximum temperatures in both IRT and oral thermometry were generally higher, but were within the IRT inaccuracy limit that suggested the elevated temperatures were mostly likely accurate and that the categorical difference of gender did not contribute to the elevation (further explored in this chapter). Environmental conditions (viz., room temperature, humidity, and wind turbidity) were continually monitored and controlled to be within the IRT manufacturer's guidance for optimal measurements, listed in chapter 3. As a result, room temperature (mean = 71.93°F, *SD*=0.75) and humidity (mean = 52.44%, *SD* = 0.59) remained steady, while

wind turbidity remained undetectable, which was favorable during IRT screening. All variables listed above showed no extreme outliers or perceived erroneous entries.

The continuous variables, oral temperature and IRT surface temperatures, were screened for skewness and kurtosis. IRT surface temperatures skewness was slightly represented (0.44) and kurtosis was insignificant (0.29, *SE* = 0.27), which rendered a relatively normal distribution. Oral temperatures skewness was slightly higher (0.50) and kurtosis was insignificant (0.13, *SE* = 0.27); although, there was some nonnormality in the data as evidenced by a recorded temperature of 102.5°F. However, transformations were not applied to the temperatures as pre-analyses using *log* and *square root* transformations resulted in increased skewness and kurtotic distributions. Notably, in a large sample (> 200 participants) minor skewness will not make a substantive difference in the analysis (Tabachnick & Fidell, 2006).

Although skewness and kurtosis do not pose significant threats to the analyses in this study, some anomalous peaks in oral and IRT temperatures should be expected as febrile outbreak conditions existed throughout the study. As such, the presence of minimal skewness may be explained by the outlier temperature of 103.2°F, as measured by IRT (mean IRT temperature = 98.21°F, *SD* = 1.14). However, this outlier shows to be true as the participant did mention feeling feverish, did not ingest antipyretics, and the difference between oral and IRT temperature readings was 0.7°F, which was within the IRT inaccuracy limits previously mentioned. Additionally, the above participant's accompanying oral temperature was the outlier in the oral temperature distribution with a reading of 102.5°F (mean oral temperature = 98.39°F, *SD* = 1.21).

With regard to the laboratory procedures, the results were reported using a double data entry protocol, which utilized two technicians entering the same diagnostic results, later screened with a computer program for similarity to increase the accuracy of data entry. Diagnostic results for the microneutralization assay were reported as seropositive (ILI positive) and seronegative (ILI negative) and matched with the sample's ship ID tag numbers unique to all MAAS crew members. PCR results were reported as positive or negative, based on viral (ILI) detection and matched with the sample's ship ID tag number. Between the two diagnostic procedures, no conflicting laboratory results were viewed when participants completed both diagnostic tests. However, when the pre-IRT screening questionnaire and diagnostic results were compared to IRT surface temperatures, some assumptions were extrapolated from the data.

For instance, one participant was categorized as a false negative in this study due to an IRT temperature < 37.5°C (99.5°F) and a positive ILI laboratory confirmation (see Figure 6). The questionnaire reported that the participant did mention feeling feverish and had recently ingested pain medication (e.g., Motrin). This could explain why the participant was not identified by IRT as febrile, due to an antipyretic interaction that lowered core and surface temperatures. A second participant was categorized as a false negative due to an IRT temperature <37.5°C (99.5°F) and a positive ILI laboratory confirmation. The questionnaire reported that the participant did not have a history of feeling feverish, had no ingestion of antipyretic medication, but received the current seasonal influenza vaccination. As a result, vaccine induced seroconversion was most likely detected and not due to a recent ILI. Another participant was categorized as a false positive due to an IRT temperature ≥37.5°C (99.5°F) and a negative ILI laboratory

confirmation. The prescreening questionnaire reported no ingestion of antipyretic medication or seasonal vaccination, although the participant mentioned feeling feverish prior to being screened by IRT. This might be explained by an early onset of a febrile symptom (ILI induced) with undetectable viral shedding, indicating early infection, or inadequate time for positive seroconversion as both PCR and microneutralization assay results were shown negative for ILI. Finally, a fourth participant was categorized as a false negative due to an IRT temperature <37.5°C (99.5°F) and a positive ILI laboratory confirmation. The questionnaire reported that the participant did not feel feverish, did not have the seasonal influenza vaccine, but did recently ingest antipyretic medication for pain. These results might have suggested inapparent infection with ILI and/or the antipyretic medication effects that lowered the core and surface temperatures that allowed the participant to be undetected by IRT. The next section will address the research questions and hypothesis explored in this dissertation.

Research Questions and Hypotheses

For the purpose of clarification, the narrative below and statistical analysis for research question one were derived from the 2x2 epidemiological box plot (see Table 6) that used IRT surface temperatures, and diagnostic PCR and serological confirmatory results to determine true positives, false positives, true negatives, and false negatives. Sensitivity, the true positive rate for this study was 84.5% and specificity, the true negative rate, was 97.5%. The false positive rate was 2.5% and the false negative rate was 15.5%. Research question one drew upon the true positive rate (84.5%) vs. false positive rate (2.5%) that was used in the ROC analysis, further explained below.

Table 6

IRT Surface Temperature versus Disease Confirmation

	ILI (+)	ILI (-)
IRT ≥ 99.5°F (37.5°C)	71	6
IRT < 99.5°F (37.5°C)	13	230
Total	84	236

Research Question 1

Can IRT, in a mass screening shipboard environment, statistically differentiate between afebrile participants without ILI exposure and febrile participants with ILI exposure?

ROC Analysis of Research Question 1

Figure 8 provides the ROC analysis for this study. As mentioned in chapter 3, ROC analysis is a test of perfect discrimination when no overlap in the two distributions (true positive rate vs. false positive rate) is observed. Perfect discrimination can be observed when the ROC plot passes through the upper left corner (i.e., 100% sensitivity and 1-specificity [ROC=1.0]) of the graph. The greater AUC, the better average ability of IRT to differentiate between febrile (with ILI) and afebrile (without ILI) participants.

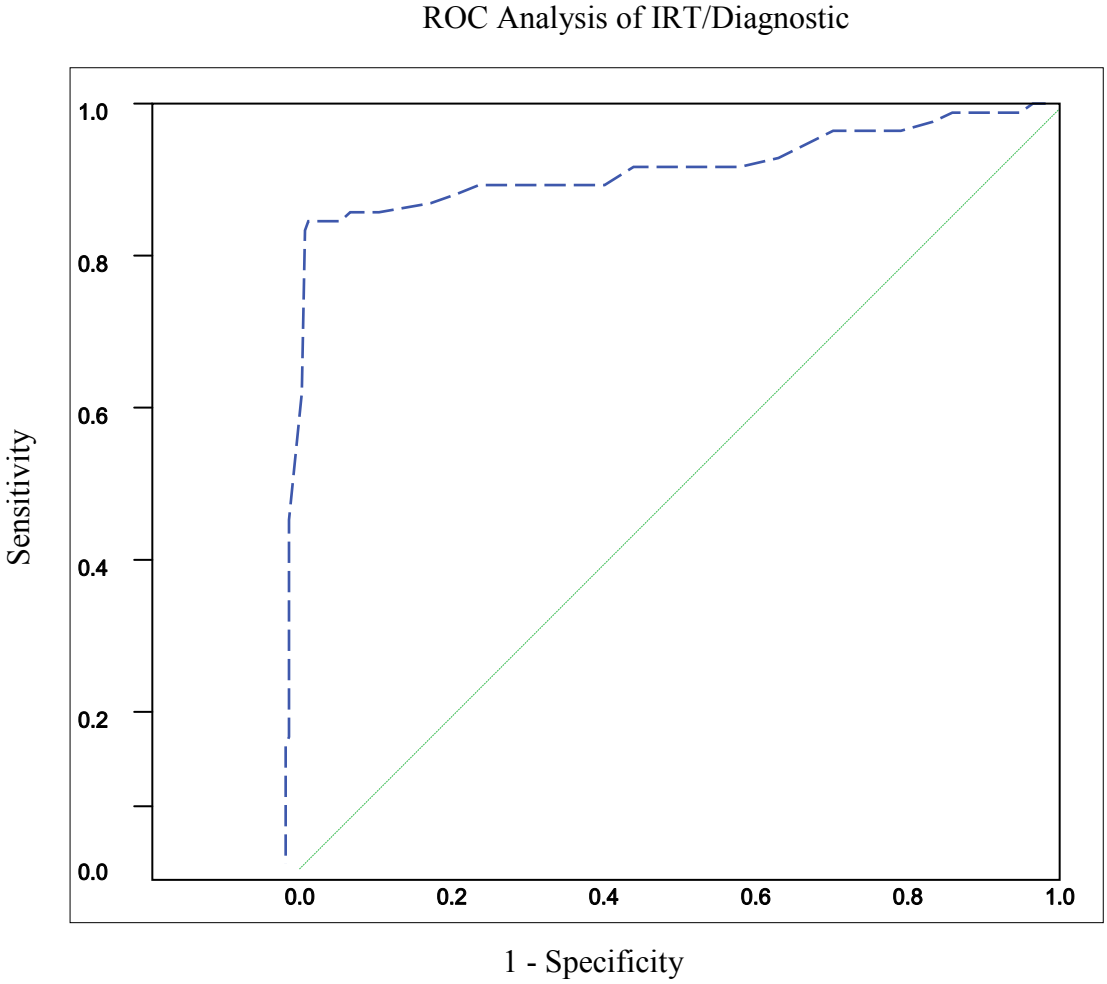

Figure 8. ROC curve of TPR versus FPR (ROC = 0.91, 95% CI [0.861 - 0.957]). The diagonal line represents a ROC = 0.50 (i.e., failed differentiation), or viewed as a 50:50 chance that IRT can differentiate between an individual who is febrile (with ILI) and an individual who is afebrile (without ILI).

As viewed above, the ROC analysis output was 0.91 (close to the ideal value of 1.0), which was defined in chapter 1 as excellent differentiation between febrile (with ILI) and afebrile (without ILI) participants. This plot can be interpreted as meaning a randomly selected individual from a positive group (i.e., febrile individuals' with ILI) has a temperature greater than that of a randomly selected individual from a negative group (i.e., afebrile individuals' without ILI) 91% of the time. Additionally, in order for IRT to

be considered efficacious it requires sensitivity ≥80% and specificity ≥75% (see chapter 1; Hanley & McNeil, 1982; Ng, Kaw, & Chang, 2004; Swets, Dawes, & Monahan, 2000). Aforementioned in this section, IRT sensitivity of 84.5% and specificity of 97.5% were both achieved in this study; when coupled with the statistically significant ROC output of 0.91, IRT efficacy was confirmed in this study. To further develop how these findings pertain to the research question, a review of the alternative and null hypotheses is warranted.

Research Question 1 Hypotheses

H_A1: In a mass screening shipboard environment, there is an association between individuals identified as febrile by IRT and individuals identified as having ILI through laboratory confirmation.

H_01: In a mass screening shipboard environment, there is no association between individuals identified as febrile by IRT and individuals identified as having ILI through laboratory confirmation.

H_A2: In a mass screening shipboard environment, there is an association between individuals identified as afebrile by IRT and individuals identified as not having ILI through laboratory confirmation.

H_02: In a mass screening shipboard environment, there is no association between individuals identified as afebrile by IRT and individuals identified as not having ILI through laboratory confirmation.

The ROC analysis was used to determine the association between febrile (with ILI) and afebrile (without ILI) IRT screened participants. As a result, an excellent

association was determined by a ROC output of 0.91, with 1.0 being the highest association and 0.5 being statistically insignificant. In other words, IRT screening associated febrile participants with ILI and afebrile participants without ILI, on average, approximately 91% of the time. After performing *chi square* analysis at the 0.95 confidence level (df =1), χ^2 was statistically greater than the critical value of 3.84 (χ^2 = 230.71, p = < 0.01), which suggested acceptance of the alternative hypotheses (H_A1 and H_A2) and rejection of the null hypotheses ($H_0 1$ and $H_0 2$).

Research Question 2

Does the relationship between oral and IRT surface temperatures vary by gender; in other words, does the efficacy of IRT for screening and identifying subjects with ILI differ between males and females?

Pearson's Correlation Analysis of Research Question 2

A Pearson's product-moment correlation coefficient (PMCC) was used to measure the degree of a linear relationship by gender between oral temperature and IRT surface temperature. First, the relationship was investigated for males and females separately using the PMCC. There was a strong correlation between the two variables for males (r = 0.90, n = 226, p < 0.01; see Figure 9) and females (r = 0.87, n = 94, p < 0.01; see Figure 10) with higher oral temperatures associated with higher surface temperatures (male t = 30.91, p < 0.01; female t = 16.92, p < 0.01).

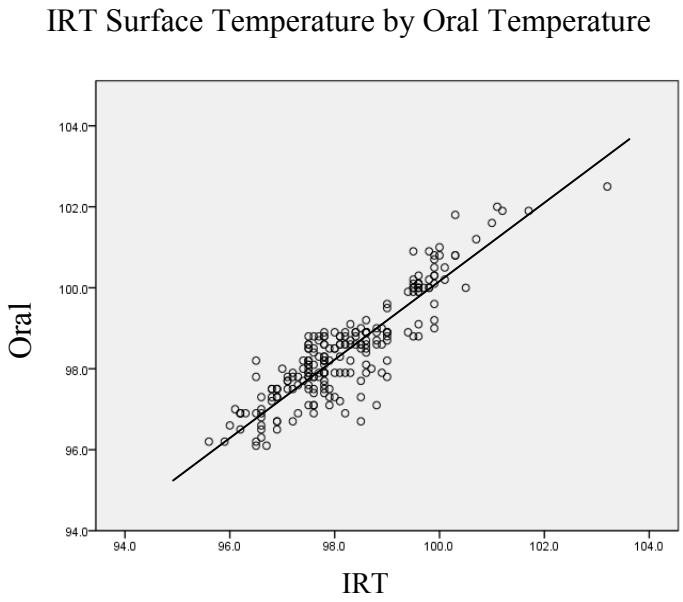

Figure 9. Male IRT surface temperature by oral temperature ($r = 0.90$, $p < 0.01$).

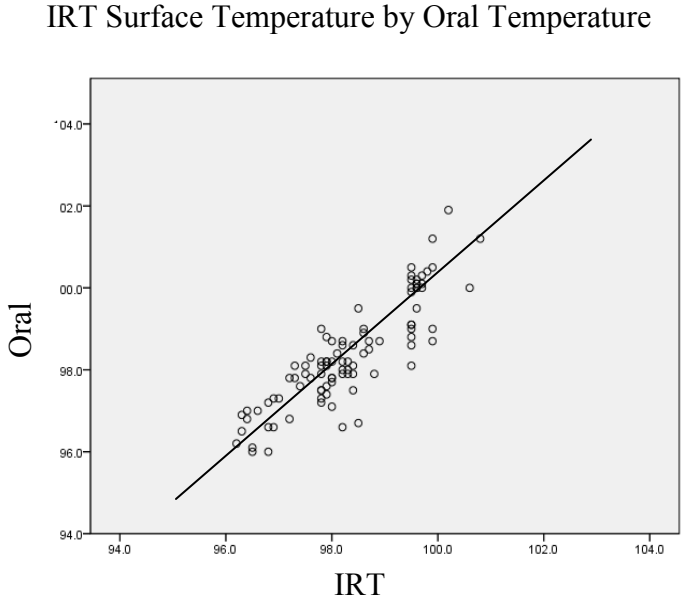

Figure 10. Female IRT surface temperature by oral temperature ($r = 0.87$, $p < 0.01$).

Moreover, a Fisher's transformation was applied to change the *r*-values into *z*-values. The *z*-value for males was computed to be 1.47 (*SE* = 0.07) and the females was 1.33 (*SE* = 0.10). An observed *z*-value was then computed to compare the differences between male and female correlations. The observed *z*-value was 1.12 (*SE* = 0.26), which suggested there was not a statistically significant difference (viz., significance = $z \leq -1.96$ or $z \geq 1.96$) in the strength of the correlation between IRT surface and oral temperatures for both males and females

Research Question 2 Hypotheses

H_A3: The relationship between oral and IRT surface temperatures does vary by gender.

$H_0 3$: The relationship between oral and IRT surface temperatures does not vary by gender.

Regarding Figures 9 and 10, no observable variance existed between IRT surface temperatures and oral temperatures between the genders. Statistically, when the observed *z*-value was computed the quantifiable difference in the strength of the correlation between IRT surface and oral temperatures for males and females was expressed (1.12). At the 0.05 level of significance, $z \leq -1.96$ or a $z \geq 1.96$ is statistically significant. The finding suggested that the null hypothesis ($H_0 3$) could not be rejected, as the variance between IRT surface and oral temperatures for males and females was statistically insignificant.

Summary and Transition

This chapter presented the results of the analyses used to test each of the research questions and hypotheses generated for this study. In the first research question, the alternative hypothesis was accepted. The conclusion to this question revealed excellent efficacy when using fixed IRT for identification of subjects with ILI. In the second research question, the null hypothesis was not rejected. As a result, no statistically significant difference in the strength of the correlation between IRT surface and oral temperatures for males and females was found.

Chapter 5 will provide a summary of the interpretation of the findings presented in this chapter. Additionally, recommendations for further study will be addressed, strengths and limitations highlighted, and implications for social change will be presented.

Chapter 5: Conclusions

This study was conducted to research the efficacy of fixed IRT for identification of subjects with ILI. Past studies have primarily explored IRTs ability to function as a proxy to clinical thermometers for estimating core temperature, not as a means of screening individuals for ILIs (Chiang et al., 2008). This research was grounded through the use of a conceptual framework that was derived from former IRT studies that focused on anatomical regions to screen for the highest thermal yield, the control of environmental influences that affected IRT measurements, and IRT temperature correlation with clinical thermometry. This study specifically compared clinical diagnostics of sampled IRT participants to confirm the absence or presence of ILI to explain if IRT identified only febrile subjects with ILI or all subjects with elevated surface temperature (with or without ILI exposure). The current study also compared IRT surface temperatures and oral temperatures between males and females. Previous IRT research had identified a discrepancy between surface and core temperature measurements by gender (Nguyen et al., 2009; Ring et al., 2008). Gender core and surface temperature differences could pose a significant impediment of this technology if IRT cannot objectively measure surface temperature equally in males and females, or if adjustments in those differences cannot be made.

Summary and Interpretations of Findings

In relation to the first research question, whether or not IRT can statistically differentiate between afebrile participants without ILI exposure and febrile participants with ILI exposure, it was hypothesized that there was an association between individuals identified as febrile by IRT and individuals identified as having ILI through laboratory

confirmation. A statistically significant ROC output of 0.91 (95% CI [0.861-0.957]) was determined in support of the alternative hypothesis. This output can be interpreted as meaning a randomly selected individual from a positive group (i.e., febrile individuals' with ILI) has a temperature greater than that of a randomly selected individual from a negative group (i.e., afebrile individuals' w/out ILI) 91% of the time. This result suggests that IRT has excellent ability to differentiate between afebrile (without ILI) and febrile (with ILI) individuals in a mass screening shipboard environment. Moreover, this finding is in support of Nguyen et al.'s (2009) and Ng et al.'s (2004) research, which had favorable ROC output conclusions of 0.96 and 0.97 (see Table 2) in similar studies, yet clinical lab confirmation was not used in their study design.

Question 2 investigated the relationship between oral and IRT surface temperatures by gender. There was a strong correlation between the two variables for males ($r = 0.90$, $p < 0.01$; see Figure 9) and females ($r = 0.87$, $p < 0.01$; see Figure 10) with higher oral temperatures associated with higher surface temperatures (male t-value 30.91, $p < 0.01$; female t-value 16.92, $p < 0.01$). The outcome was in favor of the null hypothesis and quantifiably showed that IRT can be used as a proxy to oral thermometry due to the strong correlation and insignificant variance in temperature between the genders correlations (*observed* $z = 1.12$, $SE = 0.26$). However, this finding was not supportive of a past IRT study that examined the gender IRT surface and oral temperature association (viz., Nguyen et al., 2009). Specifically, Nguyen et al. (2009) identified gender as a possible covariate, as the male average surface temperatures were slightly higher (0.2°F) than female surface temperatures on all three IRT cameras used in their study. Their study suggested the potential influences of body fat composition, facial hair,

or facial cosmetics that may have contributed to the variance between the genders. These variables were not directly examined in the current study. Due to the military population used in this research, fat composition in general should be lower, as weight restriction and physical fitness requirements are strictly enforced throughout the services; facial hair is not allowed; and facial cosmetics are restricted for use in uniform. Therefore, these variables were not observed in this study, and the selected population allowed for the examination of the gender and temperature association without the previously mentioned confounders.

In alignment with this research, Ring et al.'s (2008) study suggested there was no association between surface temperature and oral temperature between the genders. Of note, both studies followed similar methodologies, used equivalent IRT equipment, and controlled for environmental variables (see Table 2). However, Nguyen et al.'s (2009) study did not mention if the IRT target plane was parallel with the ground during screening, which would contribute to IRT surface temperature inaccuracies in relation to oral thermometry measurements, as the medial canthus surface temperatures may not have been captured (ISO, 2008; Ng et al., 2004). This observation could explain the variance between gender oral and surface temperatures, as the IRT may not have been properly focused on the medial canthus (highest thermal yield region) but rather on the frontal cephalic region. As mentioned in the literature review, facial cosmetics, specifically foundation, have an attenuation factor of plus or minus 0.6°C (~1.1 °F) and can typically be found on females in this region. Nguyen et al.'s (2009) participants were not excluded from using this product and this could explain why males in their study were warmer (.02°F), on average than females, as males had nothing to attenuate their

surface temperatures. These variations in study procedure may explain why Nugyen et al.'s study did not have similar results as this study and Ring et al.'s (2008) research.

Implications for Social Change

In step with the World Health Organization's *International Health Regulations* guidance, the Department of Homeland Security's *One-Health Approach to Influenza* recommendations, and the United States Department of Health and Human Services' *National Health Security Strategy* vision, there is still an unmet requirement to monitor for emerging and reemerging infectious diseases by augmenting the global capacity for disease surveillance, detection, rapid diagnosis, and reporting (Powdrill, Nipp, & Rinderknecht, 2010; USDHHS, 2009; WHO, 2005a). As shown effective for the identification of febrile (ill) subjects, IRT could be used to rapidly detect potentially infectious individuals before they come in contact with another susceptible population, which could reduce the disease burden attributed to influenza and result in positive social change that would further support public health and the previously mentioned global regulation and Federal guidelines.

In order to support positive social change through education, I designed my study to further explore IRTs efficacy for public health screening, provide direction and guidance of appropriate IRT screening equipment, and indicate limitations of the use of thermography. Additionally, the findings of this research could be used to inform senior decision makers in both civilian and military public health, which will foster informed decisions on the future use of IRT. This dissertation also serves as a comprehensive source of current, published IRT studies, including review of their shortfalls, improper/proper usages, various types of IRT equipment, how to establish an IRT station,

and discussion of ISO guidance of how these devices must be used if they are implemented for screening of febrile subjects.

Limitations and Recommendations for Further Study

Due to the military participant population in this study, some factors regarding the external validity of this research may exist. These limitations were mentioned in chapter 1 and establish the foundation of the recommendations for further research.

The military population characteristics of the study participants (viz., socioeconomic status, age, gender, and race) may make the results not easily generalizable to the general public. The characteristics of this population, however, allowed the study of IRT, a screening tool, to be directly compared to the diagnostic confirmation of disease in the participants screened, a topic no study to date has been able to explore. An attempt at the general population to recover invasive serological and viral specimens could be assumed to have an increasingly low study participation percentage (Gordis, 2004). Due to the outbreak conditions on the ship and the military public health investigation, this unique and rare study sample was gathered with only a 16% declination of participation. Following this study further, the shipboard environment was not a typical civilian health setting where IRT may be used. It would be advisable to replicate this study at a civilian port of entry, mass exodus location, or other settings as mentioned above to determine whether similar results could be found. Future IRT research could benefit from a more diverse population and a typical civilian setting where IRT screening may be put into practice.

Another limitation of the current study is that the participants' age range did not include those over age 60. Hausfater et al. (2008) mentioned age as an effect modifier

observed within the geriatric population that influenced IRT measurements. Due to the age restrictions for service in the military, Hausfater et al.'s observation was not able to be explored in this study, yet this potential limitation of IRT should be further studied. Also, preexisting medical conditions causing hyper or hypothermia were not determined prior to IRT screening. This question should be asked in future IRT studies and might account for some of the false positives and false negatives encountered in this research. However, this possible confounder is assumed to have had minimal effect on the results as most chronic medical conditions that could result in hyper or hypothermia are medical disqualifiers for entry into military service.

Finally, IRT showed excellent efficacy in an environment where a significantly elevated prevalence of disease existed (~30% prevalence; see chapter 3). A basic epidemiologic principle suggests that the higher the prevalence, the higher the predictive value of a screening test (Gordis, 2004). Consequently, any screening initiative is most proficient when it is implemented during times of elevated occurrences of disease. Continual screening during typical disease endemicity can be wasteful of public health resources, a hindrance to the public, and produce few true positives. Thus, IRT should only be utilized when the established threshold of endemic disease has been exceeded (e.g., northern and southern hemisphere flu season peaks and atypical febrile outbreaks). Recommendations for action will be explained in the next section.

Recommendations for Action

In chapter 1, IRT efficacy was defined as IRT's ability to distinguish between febrile and afebrile individuals ≥ 90% of the time (based on ROC analysis) and with a sensitivity ≥ 80% and specificity ≥ 75% (Hanley & McNeil, 1982; Ng et al., 2004; Swets et al., 2000). This study concluded with an IRT sensitivity of 84.5%, specificity of 97.5%, and a statistically significant ROC output of 91%. As a result, excellent (ROC output ≥ 0.90 - 1.0; see chapter 3) IRT efficacy was achieved. These findings support the use of IRT as an effective screening tool for the identification of individuals with ILI.

In the United States, at points of debarkation and embarkation there are limited passive and rapid surveillance means to screen travelers that might harbor infectious diseases as they enter US borders (Evans & Thibeault, 2009). These vulnerable entry points currently rely on self-reported health status surveys from travelers and reported information of evident ailing travelers from aviation crew members (John, King, & Jong 2005). These are not effective measures to reduce the burden of disease (Powdrill, Nipp, & Rinderknecht, 2010). Rapid screening and diagnostic measures must be used to further shield the public against infectious disease. As a result, IRT is one additional sentinel layer of protection that may be used in public health to rapidly screen for febrile illnesses and used at points of debarkation/embarkation, schools, and hospitals to identify infectious individuals before coming into a susceptible population.

Summary

Worldwide, public health has experienced the burden of endemic, epidemic, and pandemic infectious diseases. Febrile outbreaks of highly pathogenic H5N1, SARS, and the 2009 H1N1 pandemic influenza are recent examples that have challenged public health resources (CDC, 2010f). Self-report health status surveys from travelers, reports of evident ailing travelers from aviation crew members, and public school/State/Federal absentee reporting are not sufficient screening methods to impede the spread of febrile diseases (John, King, & Jong 2005). Public health screening ideally should include additional sentinel layers of protection (e.g., IRT) at vulnerable points where communicable disease may be easily dispersed (e.g., international/national airports, seaports, schools, hospitals, etc.).

Consequently, the efficacy of fixed IRT for identification of subjects with ILI was explored. Results showed that IRT could differentiate between febrile and afebrile participants 91% of the time (ROC = 0.91; $\chi^2 = 230.71$, $p = <.01$), indicating excellent efficacy in this study setting. The novel methods in this research allowed the clinical investigation of true positives, true negatives, false positives, and false negatives as all IRT screened participants were compared directly with their diagnostic results to confirm the presence or absence of disease. By doing so, this research allowed the examination of IRT as a screening tool for the identification of subjects with ILI, not purely the identification of individuals with elevated surface temperatures like past IRT studies have examined. Additionally, the relationship between oral and IRT surface temperatures was studied between the genders. No statistically significant difference in the strength of the correlation between IRT surface and oral temperatures for males and females was found,

indicating that IRT is likely an efficacious screening tool for both genders. In conclusion, this study provided a comprehensive review of the current IRT literature and demonstrated the efficacy of IRT in an outbreak environment to passively, rapidly, and accurately identify febrile (infectious) individuals. IRT ideally should be considered as a candidate screening tool during an emerging or reemerging febrile outbreak.

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Appendix A: PalmerWahl Information Sheet

PALMER Wahl
INSTRUMENTATION GROUP

HSI 2000S
Fever Alert Imaging System
User Manual

Wahl Instruments, Inc.
234 Old Weaverville Road
Asheville, NC 28804-1228
Phone: (828) 658-3131
1-800-421-2853
Fax: (828) 658-0728
Email: info@palmerwahl.com
Web: www.palmerwahl.com

WD1031 Rev A

Appendix B: Information Data Sheet

A Camera That Takes Your Temperature

QUESTIONNAIRE/DATA SHEET

Sex: □ Male Female

Age: ____

Ship ID Tag: _____

1. Do you have a fever now or have you felt like you had a fever in the last 24 hours?	□ Yes □ No
2. In the past 8 hours, have you taken any medicine for pain or fever, (like aspirin,Tylenol®,Advil®,or Motrin®)?	□ Yes □ No
3. Did you have the annual flu shot/nasal mist?	□ Yes □ No
Again, thank you for helping with this study.	

STUDY STAFF ONLY

Date: _____ Ship ID Tag #_____

Air Turbidity/Room temp/humidity: _____(temp ^{o}F)

Operator: _____

Source	IRT/Oral temperature
Palmer-Wahl (IRT)	
Oral Temp	

Appendix C: Data Use Agreement

DATA USE AGREEMENT

This Data Use Agreement ("Armed Forces Health Surveillance Center "MAAS" Public Health Outbreak Data"), effective as of 05 October 2010, is entered into by and between Pacific Command, Captain Chris Hinnerichs, and the Armed Forces Health Surveillance Center. The purpose of this Agreement is to provide Data Recipient with access to a Limited Data Set ("LDS") for use in research in accord with the HIPAA Regulations.

1. Definitions. Unless otherwise specified in this Agreement, all capitalized terms used in this Agreement not otherwise defined have the meaning established for purposes of the "HIPAA Regulations" codified at Title 45 parts 160 through 164 of the United States Code of Federal Regulations, as amended from time to time.

2. Preparation of the LDS. Armed Forces Health Surveillance Center shall prepare and furnish to Data Recipient a LDS in accord with HIPAA Regulations.

3. Data Fields in the LDS. No direct identifiers such as names may be included in the Limited Data Set (LDS). In preparing the LDS, Armed Forces Health Surveillance Center shall include the **data fields specified as follows**, which are the minimum necessary to accomplish the research: Public Health Outbreak investigation, MAAS PCR assay data set and Microneutralization assay data set.

4. Responsibilities of Data Recipient. Data Recipient agrees to:

    a. Use or disclose the LDS only as permitted by this Agreement or as required by law;

    b. Use appropriate safeguards to prevent use or disclosure of the LDS other than as permitted by this Agreement or required by law;

    c. Report to Data Provider any use or disclosure of the LDS of which it becomes aware that is not permitted by this Agreement or required by law;

    d. Require any of its subcontractors or agents that receive or have access to the LDS to agree to the same restrictions and conditions on the use and/or disclosure of the LDS that apply to Data Recipient under this Agreement; and

    e. Not use the information in the LDS to identify or contact the individuals who are data subjects.

5. Permitted Uses and Disclosures of the LDS. Data Recipient may use and/or disclose the LDS for its Research activities only.

Appendix D: Kestrel 4500 Information Sheet

Kestrel® 4500

Overview

For years our customers have been asking for wind direction along with wind speed. New for 2007, the Kestrel 4500 does just that with its built in digital compass. But it doesn't stop there. It also calculates crosswind and headwind/tailwind with reference to a user-set target heading, and stores the information along with all the other environmental readings in its 1400 data point memory.

Pair the 4500 Wind Meter with the Kestrel Vane Mount and you have a data-logging weather station that sets up in seconds and rotates in the slightest of breezes. Did we mention that the whole kit is the ultimate in portability? It packs down into a 2 x 6 inch pouch and weighs under 8 ounces.

Military personnel and pilots flying in darkness are often concerned with preserving their night vision. Due to overwhelming demand from our military customers, the Kestrel NV line was added in 2005.

The Kestrel 4500NV is available with an Olive Drab case or a Desert Tan case. The unit has a night-vision preserving backlight which helps users to sustain natural night vision. The NV's backlight incorporates an optical filter to reduce overall brightness and minimize blue and green spectrum light to preserve night vision. Additionally, NV backlights are also much dimmer than a standard backlight, making it more difficult to detect with the naked eye in night operations. This backlight appears soft greyish pink, not red, and is still in the visible spectrum, so is not compatible with night-vision equipment.

It takes 30 to 45 minutes for the average eye to adapt to darkness and maximize night vision. Even a short burst of white, yellow, green or blue light "bleaches out" the rod cell photoreceptors in the eye and causes night blindness until the entire adaptation process can take place again. Light in the red spectrum does not cause this "bleaching out", preventing night blindness and night vision fatigue.

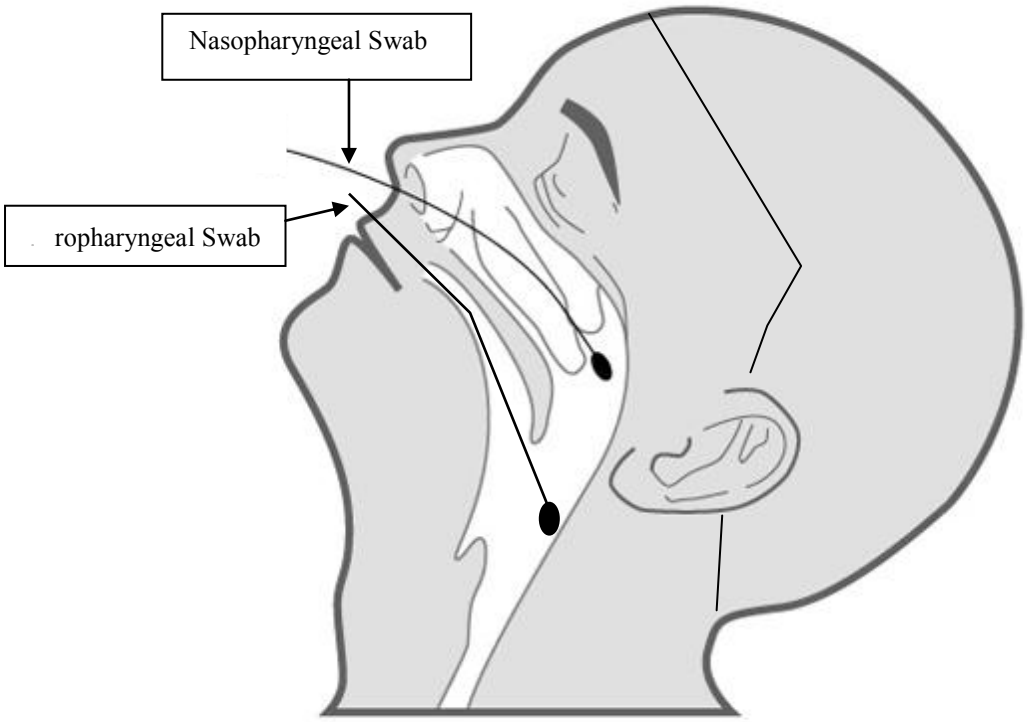
Kestrel 4500 Measures

- Heading (true & magnetic)
- Wind direction
- Crosswind
- Headwind/tailwind
- Altitude
- Pressure trend
- Barometric pressure
- Wet bulb temperature
- Relative humidity in %
- Heat stress index
- Dewpoint
- Wet bulb temperature
- Density altitude
- Wind chill
- Air, water, and snow temperature °F or °C
- Current, average, and maximum air velocity

Kestrel 4500 Features

- Waterproof and floats
- Time and date
- Easy- to-read backlit display

Appendix E: Illustration of Oropharyngeal and Nasopharyngeal Swabs



The illustration above shows placement of the nasopharyngeal and oropharyngeal swabs. Created digitally by author, 2010.

Appendix F: IRB Approval

Subject : **IRB Materials Approved-Christopher Hinnerichs**
Date : Wed, Mar 09, 2011 03:01 PM CST
From : IRB <IRB@waldenu.edu>
To : Christopher Hinnerichs <christopher.hinnerichs@waldenu.edu>
CC : Angela Prehn <Angela.Prehn@email.waldenu.edu>... more

Dear Mr. Hinnerichs,

This email is to notify you that the Institutional Review Board (IRB) has approved your application for the study entitled. "Efficacy of Fixed Infrared Thermography for Selection of Subjects with Influenza like Illness."

Your approval # is 03-09-11-0048351. You will need to reference this number in your dissertation and in any future funding or publication submissions.

Your IRB approval expires on March 8, 2012. One month before this expiration date, you will be sent a Continuing Review Form, which must be submitted if you wish to collect data beyond the approval expiration date.

Your IRB approval is contingent upon your adherence to the exact procedures described in the final version of the IRB application document that has been submitted as of this date. If you need to make any changes to your research staff or procedures, you must obtain IRB approval by submitting the IRB Request for Change in Procedures Form. You will receive confirmation with a status update of the request within 1 week of submitting the change request form and are not permitted to implement changes prior to receiving approval. Please note that Walden University does not accept responsibility or liability for research activities conducted without the IRB's approval, and the University will not accept or grant credit for student work that fails to comply with the policies and procedures related to ethical standards in research.

When you submitted your IRB application, you made a commitment to communicate both discrete adverse events and general problems to the IRB within 1 week of their occurrence/realization. Failure to do so may result in invalidation of data, loss of academic credit, and/or loss of legal protections otherwise available to the researcher.

Both the Adverse Event Reporting form and Request for Change in Procedures form can be obtained at the IRB section of the Walden web site or by emailing irb@waldenu.edu:
http://inside.waldenu.edu/c/Student_Faculty/StudentFaculty_4274.htm

Researchers are expected to keep detailed records of their research activities (i.e., participant log sheets, completed consent forms, etc.) for the same period of time they retain the original data. If, in the future, you require copies of the originally submitted IRB materials, you may request them from Institutional Review Board.

Please note that this letter indicates that the IRB has approved your research. You may not begin the research phase of your dissertation, however, until you have received the **Notification of Approval to Conduct Research** (which indicates that your committee and Program Chair have also approved your research proposal). Once you have received this notification by email, you may begin your data collection.

Both students and faculty are invited to provide feedback on this IRB experience at the link below:

http://www.surveymonkey.com/s.aspx?sm=qHBJzkJMUx43pZegKlmdiQ_3d_3d

Sincerely,
Jenny Sherer, M.Ed., CIP

Curriculum Vitae

CHRISTOPHER MICHAEL HINNERICHS

U.S. ARMY

Medical Service Corps

EMAIL ADDRESS: c.hinnerichs@us.army.mil

PRESENT POSITION: Environmental Science Officer (ESO), Epidemiology Fellow, US Pacific Command, Surgeons Office

CIVILIAN EDUCATION:

Currently – PhD(c)	Walden University, Minneapolis, MN
	Public Health (Epidemiology)
May 2006 – MS	University of New Mexico, Albuquerque, NM
	Community Health (Epidemiology)
May 2004 – BA	University of New Mexico, Albuquerque, NM
	Biology

Doctoral Studies Abroad

- March 2007 University of Andres Bello, Santiago, Chile
- June 2008 University of Liverpool, Liverpool, England

MILITARY EDUCATION:

- 2006 – 6AF5, Principals of Military Preventive Medicine, Ft Sam Houston, Texas
- 2006 – 6A11, Basic Industrial Hygiene, Ft Sam Houston, Texas
- 2006 – Emergency Responder Mass Disaster, Ft Sam Houston, Texas
- 2007 – Toxic Chemical Course, Aberdeen Proving Grounds, Maryland

MILITARY ASSIGNMENTS:

- November 27, 2008 – Current
    - Epidemiology Fellow, Force Health Protection, USPACOM, Surgeon's Office, Camp HM Smith HI
        - Duties: Oversight of Asian Pacific Rim infectious disease surveillance and reporting to the Command Surgeon General. Co-chair for the Pandemic Influenza and Infectious Disease Working Group (PIIDWG) responsible for oversight and workshop development of public health, humanitarian, and disaster relief engagements in over 32 countries, with over $12.5M in projects funded through United States Agency for International Development (USAID), Overseas Humanitarian Disaster and Civic Aid (OHDACA), and Presidential Emergency Plan for AIDS Relief (PEPFAR) projects. Action Officer for Force Health Protection (FHP) medical guidance for the Pacific Command area of responsibility that included: infectious disease threat briefs, environmental threat analysis, and vaccine/chemoprophylactic disease mitigation efforts (~325,000 personnel).

- November 27, 2006 – November 26, 2008
    - Chief Environmental Science Officer, HQ Army Materiel Command (AMC), G1 in support of Command Surgeon, Ft. Belvoir VA
        - Duties: Established Pandemic Influenza Protocol for Subordinate Commands, PI surveillance, and FHP (monitoring subordinate commands' public health, inc., exercise, nutrition, vaccination programs, mental health, smoking cessation programs). Safety Rapid Review Team member that assessed working conditions of subordinate commands for industrial hygiene surveys and occupational health support.

Strengths: General epidemiology, infectious disease epidemiology, study design and analysis, biostatistics, general environmental health

Doctoral dissertation project: "Efficacy of Fixed Infrared Thermography for Identification of Subjects with Influenza-like Illness."

Professional Affiliations:	Council of State and Territorial Epidemiologist (CSTE) International Society for Performance Improvement (ISPI) International Organization for Standardization (ISO)