

QUANTIFYING HEAT BALANCE COMPONENTS IN NEONATES NURSED
UNDER RADIANT WARMERS DURING INTENSIVE CARE

By:
Yannick Molgat-Seon

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ABSTRACT

Thermoregulation is considered a top priority in neonatology due to the fact that relative to adults, neonates have a morphological susceptibility to excessive heat exchange with the environment, and exhibit limited physiological/behavioural responses to thermal strain. Consequently, the environmental conditions in which they are nursed must be tightly regulated to maintain body temperature stable. Neonatal intensive care units (NICU) use radiant warmers (RW) to thermally manage many newborns. However, recent evidence suggests that RW induce intermittent bouts of thermal strain that could adversely affect patients. This warrants further investigation of neonatal heat balance and the pertinent factors affecting it. Conducting an exhaustive audit of heat exchanges affecting the body during standard care under a RW could yield important information that would lead to the improvement of clinical practice in NICUs. The present thesis focuses on neonatal thermoregulatory responses, various body heat exchange mechanisms and processes during standard care under RW.

OPERATIONAL DEFINITION OF TERMS

<i>Neonate:</i>	Represents a newborn infant in the first 28 days of life.
<i>Gestational Age (GA):</i>	Refers to the age of a fetus at birth from the time of conception.
<i>Full-Term Neonate (FT):</i>	The World Health Organization defines as full-term neonate as a newborn with a gestational age = > 37 weeks.
<i>Pre-Term Neonate (PT):</i>	The World Health Organization defines a neonate as pre-term or premature when the birth occurs between the 22nd and the 37th week of gestation.
<i>Low Birth Weight Neonate (LBW):</i>	Neonates with a birth weight of less than 2500 g.
<i>Neonatal Intensive Care Unit (NICU):</i>	A unit of a hospital specializing in the care of ill or premature newborn infants.
<i>Ambient Temperature:</i>	Refers to the temperature of one's surroundings.
<i>Core Temperature:</i>	Refers to deep body temperature, or temperature of vital organs including the brain.
<i>Shell Temperature:</i>	Refers to the temperature of the outermost layer of the body in contact with the external environment, or skin temperature.
<i>Cold Strain:</i>	Reduction in core temperature due to a bout of cold stress.
<i>Cold Stress:</i>	State wherein the rate of heat loss to the environment exceeds that of heat produced within the body due to environmental parameters.
<i>Heat Strain:</i>	Increase in core temperature due to a bout of heat stress.
<i>Heat Stress:</i>	State wherein the rate of heat produced within the body exceeds that of heat lost to the environment due to environmental parameters.
<i>Transepidermal Water loss (TEWL):</i>	Water that passes from inside a body through the skin to the surrounding atmosphere via diffusion and subsequent evaporation.
<i>Insensible Water Loss (IWL):</i>	A quantity of water that passes from inside a body to the surrounding atmosphere via diffusion through the skin and subsequent evaporation as well as via evaporation from the respiratory tract. Newborns have little physiological control over this process.

**PART ONE: EMPIRICAL, THEORETICAL AND METHODOLOGICAL
CONSIDERATIONS**

I. INTRODUCTION

Background

It is well known that as homeotherms, humans require the maintenance of a stable core body temperature at a “set-point” of $\sim 37^{\circ}\text{C}$ to ensure the optimal functioning of essential enzymatic reactions and fundamental physiological processes (1-4). Despite its relative stability, core temperature does deviate according to the body’s circadian rhythm to the order of $\pm 0.5^{\circ}\text{C}$, however, any greater deviation from the body’s operating temperature can ultimately lead to a number of deleterious effects on overall health (5). Hypothermia, a condition defined as a core body temperature lower than 35.0°C (10), has been recognized as a significant contributor to neonatal morbidity and mortality in developing as well as developed countries (11, 12). Furthermore, prolonged hypothermia has been linked to the manifestation of hypoglycemia, respiratory distress, hypoxia, metabolic acidosis (13, 14, 15) and overall negative clinical outcomes in neonates (16). Inversely, hyperthermia can also be harmful to a newborn’s health. While the criteria for defining hyperthermia in neonates is not well established, its effects have been heavily documented (58). Febrile neonates have higher rates of morbidity and mortality as well as sepsis (59). Furthermore, hyperthermia has been associated apnoeic episodes and even sudden infant death syndrome (92, 93). Although much less prevalent, hyperthermia is still considered an important risk for newborn infants. The increased risk of significant changes in core temperature in newborns relative to adults can be attributed to two distinct factors, an immature thermoregulatory system and a morphological susceptibility to excessive heat exchange (5).

Prenatally, the fetus plays a very passive role in maintaining normothermia but immediately following birth, the transfer from the womb's thermoneutral environment to a cooler, more variable environment, requires them to have developed thermoregulatory responses in order to control internal body temperature and stave off any resultant thermal strain (2). Yet, unlike adults, neonates do not have sufficiently mature thermoregulatory systems to allow them to cope with changes in their thermal environment (6). To ensure the safety of an infant immediately following birth, it has been recommended that delivery rooms be kept at an ambient air temperature of 25°C, however, for the infant this still poses a reduction in ambient temperature of ~12°C which can lead to a rate of heat dissipation that exceeds metabolic heat production resulting in a reduction in core temperature (4, 7, 8, 9). Thermoregulation must therefore be externally provided by the caregiver, but without an accurate feedback mechanism, thermal management could lead to an inadvertent increase in core temperature, which could lead to hyperthermia. Indeed, without adequate thermal management a neonate's core temperature can regularly deviate significantly from the set point of ~37°C.

Core temperature changes have been shown to be more prevalent in pre-term [PT] infants as well as infants with a low birth weight [LBW]. While full-term [FT] infants have a relatively good ability to adapt to the thermal changes in their environment, PT and LBW infants have greater difficulty due to physiological and morphological factors. As such, the prevalence of hypo/hyperthermia in this population is much greater (17). The *EPIcure* study, a large prospective observational study conducted in the United Kingdom and Ireland, evaluated the outcomes of PT infants in an effort to describe survival and health problems in this population. The results demonstrated that, upon

admission to the neonatal intensive care unit [NICU], 40% of the infants were hypothermic and were in more critical condition than were those with normal temperatures (3). Since hypothermia has been shown to increase the propensity for poor health, it is clear that thermal management is an essential component to postnatal care. In light of these facts, the World Health Organization (WHO) has listed hypothermia as one of the “top killers” during the neonatal period (4).

It is therefore clear that advances need to be made in order to mitigate the onset of core temperature changes, thereby reducing the prevalence of negative clinical outcomes associated with hypo/hyperthermia. This can only be achieved by rigorously investigating the thermal human/environmental heat exchanges environment in an NICU setting.

II. LITERATURE REVIEW

Human Thermoregulatory System

The human thermoregulatory system consists of central and peripheral thermoreceptors, afferent pathways and an integration point into the central nervous system (18). This system allows the body to detect changes in its thermal status due to environmental parameters. Peripheral thermosensors consist of free nerve endings distributed below the skin surface that detect changes in temperature of body's shell. These receptors are selectively sensitive to heat or cold and are stimulated at different levels depending on the temperature on the tissue they innervate (68). This feedback gives the brain a relatively rapid indicator of the thermal status of the body's shell that is used to initiate thermoregulatory responses. In contrast, central thermosensors, found within the body in structures such as visceral organs, the spinal cord and the hypothalamus, detect changes in "core" body temperature (49). Information regarding any changes in temperature, whether in the body core or shell, will be sent as nerve impulses via afferent pathways as feedback responses to the hypothalamus. Serving as the central regulating structure of the thermoregulatory system, the hypothalamus is responsible for initiating necessary thermoregulatory responses in reference to afferent feedback (1, 19). These responses invoke concomitant changes in sympathetic nervous system activity, which elicits endocrine reactions in order to provoke physiological and behavioural responses to the ambient environment. These responses are essential in maintaining a stable core temperature by modifying avenues of human/environmental heat exchange.

Thermoregulatory Responses

In order to maintain a stable core temperature, the body must be able to respond quickly to environmental changes. Thermoregulatory responses are initiated in reference to whether the body is experiencing cold or heat strain. A reduction of body temperature is the result of cold stress wherein the rate of heat loss to the environment exceeds that of heat production within the body (7). The posterior hypothalamus, responsible for initiating response to cold strain, detects these changes and initiates a specific sequence of responses (1). First, by reducing peripheral blood flow through vasoconstriction, heat distributed in the periphery is shunted towards the core in an effort to mitigate heat loss from the skin by reducing the temperature gradient between the skin and the ambient air. At a lower skin temperature, the body experiences significantly lower rates of dry heat loss to the environment. Secondly, there is an initiation of shivering which causes an increase in metabolic heat production. Throughout this process, we can also observe behavioural adaptations to cold where the body seeks sources of heat and reduce heat loss (i.e. clothing or posture) (20, 51). As a result of these responses, the body manages to stave off extended bouts of cold strain that eventually lead to hypothermia. During heat strain, body temperature begins to rise and stimulate core/skin thermosensors. This time, the anterior portion of the hypothalamus responds by initiating heat strain responses based on this central and peripheral feedback (1). Initially, vasodilatation is stimulated causing a redistribution of body heat content to the periphery, which subsequently increases the body's shell temperature. In doing so, the body's heat content is distributed over a greater surface area, which increases skin temperature thereby elevating the rate of dry heat loss to the ambient environment (64). Secondly, the body triggers a sweat

response, raising the amount of heat loss via evaporation by increasing the level of humidity at the skin surface.

It is important to note that despite their relatively inefficient thermoregulatory responses, neonates have the ability to respond to changes in their thermal environment in the same way as adults with the exception of two important factors [Figure 1] (20, 21). During cold strain, adults heavily rely on shivering thermogenesis and behavioural adaptations, however, these responses are non-existent in neonates (2, 69, 70). Newborn infants adapt to cold strain via two principal avenues, peripheral vasoconstriction and non-shivering thermogenesis (2, 3, 5, 22, 23). Although these mechanisms are effective in resisting changes in core temperature, the fact neonates possess limited cold strain responses significantly limits their ability to respond to prolonged exposure to a cold environment. In addition, Kroth *et al.* found that their vasomotor activity and skin blood flow are limited. When comparing various vascular parameters in neonates relative to adults, neonates were found to have significantly lower levels of functional small vessel density, which further increases their susceptibility to thermal strain since they have a blunted capacity to redistribute heat (24). Furthermore, neonates have been shown to demonstrate lower sweat rates than adults. Foster *et al.* describe that newborns exhibited sweat responses three fold lower than a cohort of adults using a *Perspex* capsule placed on the anterior portion of the mid thigh (63). It is speculated that PT neonates possess an even lower capacity to sweat in response to heat strain in reference to FT neonates (72). In spite of this, newborns are susceptible to greater TEWL, which serves as a passive (i.e. uncontrolled) compensation for lack of sweating, but consequently predisposes them to excessive heat and water loss. While sweating is controlled through stimulation and

inhibition, TEWL occurs independently of autonomic response via diffusion through the epidermis.

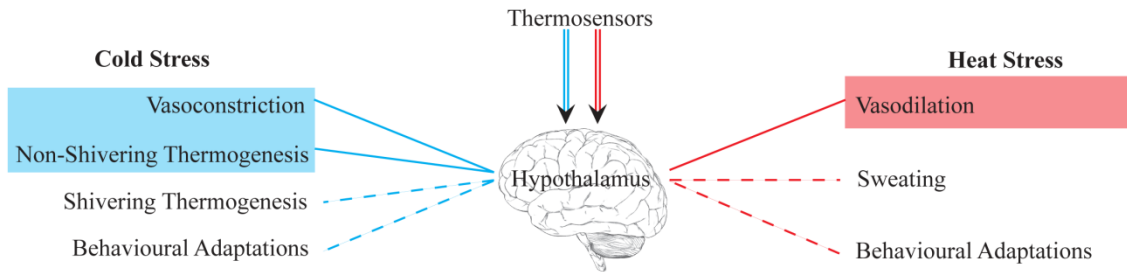


Figure 1. Physiological response to cold and heat stress in humans, dashed lines indicate response that neonates have little or no ability to produce relative to adults and highlighted factors indicate the main cold stress and heat stress responses in newborns.

Morphological Characteristics

While immature thermoregulatory responses are an important predisposing factor for significant core temperature changes, it is essential to note that heat generated within the body or gained by passive transfer with the external environment is directly influenced by the thermophysical properties of the body (71). A neonate’s morphological characteristics such as skin thickness, tissue insulation and body surface area-to-mass ratio, also render it susceptible to thermal strain. These inherent characteristics, unique to every individual, directly influence the magnitude of heat exchange between the body and the external environment.

The structural properties of premature neonatal skin are significantly different from those of the FT neonate (62). It is generally considered that the epidermis has developed a reasonable level of functionality from about the 34th week of gestation (61). Consequently, neonates born prematurely exhibit lower thickness and altered structure of the *stratum corneum*, the outermost layer of the human epidermis. As such, their skin has a high level of permeability to heat and water (25). Thus, evaporative heat loss through

the skin is markedly greater in PT neonates than in FT neonates (26). As we will discuss later on, it has been shown in several studies involving neonates in an intensive care setting that TEWL is a significant factor in total heat loss (20, 27, 28). Along with lower skin thickness, it is important to consider tissue insulation since neonates have lower levels of subcutaneous fat stores (22). Less tissue insulation reduces the resistance to heat transfer from the body core to the skin thereby increasing the skin-to-air temperature gradient and increasing dry heat exchange to the environment. Furthermore, the combination of a lower skin thickness and tissue insulation affects the temperature gradients within the body. While it is known that a significant gradient exist between the skin surface and core internal organs in adults, it is well known that in neonates, this same gradient is less pronounced [Figure 2A]. Lastly, neonates have a very high surface area-to-mass ratio, which means that a greater area of tissue is exposed to the ambient air for both dry and evaporative heat exchange [Figure 2B] (29). Since the rate of heat exchange is directly proportional to body surface area in relation to total mass, neonates have a larger interface for human-environmental heat exchange relative to total thermogenic mass. As such, the potential rate of heat exchange per unit of mass is much greater in newborn infants relative to adults.

By virtue of these three factors, it is clear that neonates are more “*thermally passive*” than adults. They cool down or heat up more liberally and have a limited capacity to actively defend core temperature than adults, even under moderate environmental conditions. It is therefore clear that neonates require special attention with regards to their thermal environment in order to ensure good health, proper growth as well rapid recovery. Given the fact that thermal strain can be so harmful to a neonate’s

health, considering both thermoregulatory mechanisms and body morphology is an essential component of thermal management during neonatal intensive care.

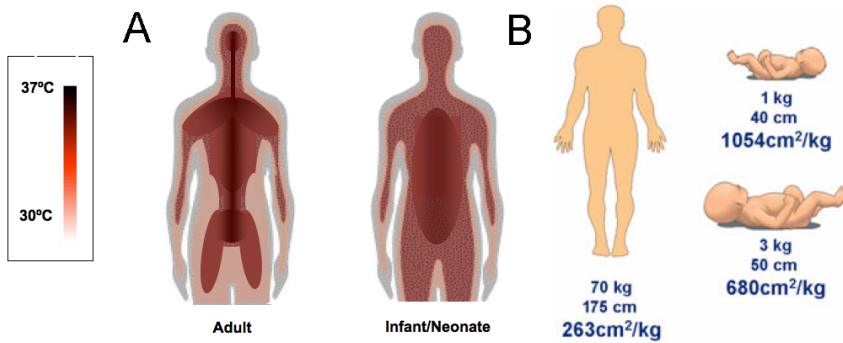


Figure 2. [Adult vs. Neonate] (A) Thermographic Imaging, (B) Surface area-to-mass ratio.

Human Heat Balance

One of the main goals of the NICU is to maintain a thermoneutral environment to promote growth, development and recovery for in-patients. By definition, a thermoneutral environment is one in which core body temperature is maintained not by active thermoregulatory responses, but by passive mechanisms of heat exchange (2, 32). This can be justified by the fact that neonates, especially PT and LBW neonates, can only exhibit active thermoregulatory response for a short period of time without limiting the amount of energy they devote to growth and development (6). A thermoneutral environment is achieved by way of balancing the rate at which heat is lost to the environment (i.e. heat balance) with the rate at which heat is produced within the body, resulting in minimal heat storage, thus keeping the total energy required to thermoregulate as low as possible. This refers a concept known as human heat balance that is summarized by (1):

Conceptual Equation

$$M - W = (\pm K \pm C \pm R) + E (\pm S) \dots \dots \dots W/m^2 \dots \dots \dots (\text{Eqn. 1})$$

Where: [M] is the metabolic energy expenditure, [W] is the rate of external work, [K] is the rate of heat exchange by convection, [C] is the rate of heat exchange by conduction, [R] is the rate of heat exchange by radiation, [E] is the rate of heat loss by evaporation; and [S] rate of net heat storage.

It is important to note that while heat balance may still be achieved at very high or very low core temperatures, the concept of thermoneutrality refers specifically to a situation where heat balance is met at a neutral internal temperature of approximately 37°C with a minimal metabolic rate.

The first law of thermodynamics states that energy is conserved in any process involving a thermodynamic system and its surroundings. As such, total internal energy within this system can be divided into components of heat and work. Thermal stasis is achieved by way of balancing metabolic heat production with total heat loss via its four distinct avenues, K, C, R and E [Figure 3].

Metabolic Heat Production

For humans, total metabolic energy expenditure, which represents the total amount of energy consumed by the body in order to accomplish various internal processes, can be broken down into metabolic heat production and external work. Metabolic heat production represents the total amount of energy released as heat whereas external work represents any physical movement that can be the product of said energy consumption. Thus metabolic heat production can be determined by the difference between total metabolic energy expenditure [M] and the amount of energy used to accomplish external work [W]. For the purpose of our research, the external work component of this equation is considered negligible. This is attributed to the fact that no energy consumed (i.e. total metabolic rate) will be used for external work as neonates in

an NICU setting are almost exclusively at rest and thus, external work must not be subtracted from total metabolic rate. Therefore the proportion of total energy expenditure directly used to perform external work is virtually zero.

Conduction

Conduction represents a transfer of heat between two solid surfaces in direct contact with one another. The rate of conductive heat transfer is in direct proportion with the temperature gradient between the skin surface and the solid with which it is in contact as well as to the conductivity of the material in question. This heat exchange avenue can be defined mathematically according to the following equation:

$$K = h_k (T_{sk} - T_{Surface}) \dots \dots \dots W/m^2 \dots \dots \dots (Eqn. 2)$$

Where: $[h_k]$ represents the thermal conductivity of the material in contact with the body, $[T_{sk}]$ the temperature of the skin and $[T_{Surface}]$ the temperature of the solid surface in contact with the body.

Convection

Convection is defined as the transfer of heat from a given body promoted by the movement of a given non-solid medium. In the case of whole-body heat balance, this medium is typically air. The rate of convective heat transfer is directly proportional to the temperature gradient between the skin and the ambient environment. Furthermore, convection has a direct relation to the velocity of the medium (i.e. air) passing over the body. Mathematically, convective heat transfer can be expressed by:

$$C = h_c (T_{sk} - T_a) \dots \dots \dots W/m^2 \dots \dots \dots (Eqn. 3)$$

Where: $[h_c]$ represents the convective heat transfer coefficient, determined by air velocity, $[T_{sk}]$ the temperature of the skin surface and $[T_a]$ the temperature of ambient air.

Radiation

Radiation can be summarized as the electromagnetic energy transfer directly from one body to another. When considering radiative heat transfer it is important to note that it's magnitude is directly proportional to several factors; the difference between the temperature of the outer surface of the body and mean radiant temperature of the ambient environment, the distance between the two radiative sources, the emissivity of the object/body, as well as and the effective radiative area of the body, determined by the posture of the person and the orientation of the person relative to the radiation source. As such, it can be defined mathematically as:

$$R = h_r (T_{sk} - T_a) \dots \dots \dots W/m^2 \dots \dots \dots (Eqn. 4)$$

Where: $[h_r]$ is radiative heat transfer coefficient determined by emissivity and effective surface area, $[T_{sk}]$ is the temperature of the skin surface and $[T_a]$ the temperature of the air. Just as it is the case for convection, the difference between T_{sk} and T_a represents the gradient between skin and air temperature.

Evaporation

Heat loss by evaporation occurs due to a difference in the partial pressure of water vapour between the skin surface and ambient air. Generally speaking, for the purpose of whole body heat balance within an NICU setting, we can conclude that negative evaporative heat loss via condensation is negligible. Thus, evaporative heat transfer from the body is always considered negative (i.e. evaporative heat loss). The rate of evaporation is directly proportional to the partial pressure gradient of water vapour as well as air velocity surrounding the body. Evaporative heat loss can be defined mathematically as:

$$E = h_e (P_{sk} - P_a) \dots \dots \dots W/m^2 \dots \dots \dots (Eqn. 5)$$

Where: $[h_e]$ represents the evaporative heat transfer coefficient – calculated based on convective heat transfer coefficient (h_c), i.e. air velocity, and the Lewis Relation, $[P_{sk}]$ represent partial

pressure of water vapour at the level of the skin and $[P_a]$ partial pressure of water vapour in the air.

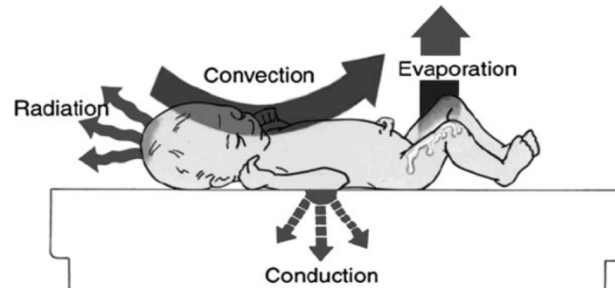


Figure 3. Heat exchange avenues in neonates (69).

In a normothermic state, the body can maintain a stable core temperature by balancing the rate of metabolic heat production with the rate of net heat loss to the environment by modulating various aspects of the heat balance equation through thermophysiological responses. In adults as well as neonates, this equation represents a complete audit of heat exchanges between the body and the external environment. Applied to an NICU setting, the human heat balance equation offers invaluable information that can be used to optimize thermal environment and contribute to reducing heat imbalance and subsequent variation in core temperature in this population.

Neonatal Intensive Care

The first week of life is considered critical in neonates (30, 50). For PT and LBW infants, the first portion of their lives can be an immense challenge during which they must adapt to an adverse external environment. These infants are typically admitted into intensive care to be monitored until they are healthy enough to be discharged. During their stay, the ambient environment in which they are kept is tightly regulated to allow optimal conditions for growth and recovery. Extensive research has been conducted on

thermal management techniques within the NICU, however there is little consensus regarding which methods confer the greatest advantages. Despite the current trend towards a reduction in infant morbidity and mortality in NICUs, there is still much room for improvement (16). The following section of this review will focus upon current findings surrounding the neonatal thermal environment within the NICU and bring special attention to the various components of human heat balance.

Thermal Management devices in the NICU

Prior to investigating heat exchange in neonates it is essential to understand the two main thermal management devices employed within modern NICUs; incubators and radiant warmers [Figures 4 & 5]. Since their inception in the 1950's, several thermal management strategies have been employed within NICUs, from the most rudimentary such as skin-to-skin contact provided by the mother, to the most advanced, such as incubators and radiant warmers (33, 53). While strategies such as skin-to-skin contact have been shown to be relatively effective, NICUs consistently favour external thermal management devices since they promote the maintenance of a thermoneutral environment. Radiant warmers are beds open to the ambient air with a radiant heat source pointed towards the infant directly above them (27). The flux of radiant heat is servo-controlled using a skin temperature recorded by a transcutaneous probe placed on either the liver or axilla at a set temperature of 36.5 °C. Any deviation from this set point provokes a negative feedback response from the radiant heater that contributes to maintaining skin temperature stable. The overall aim of the radiant warmer is to mitigate excessive heat loss from the body to the surrounding environment by providing thermal aid in the form of an external radiant heat load. This method is particularly effective since

radiative heat exchange is one of the most significant heat loss avenues in neonates. Incubators on the other hand are horizontal beds equipped with a transparent plastic hood with various access ports and a warming device positioned under the bed surface. Air is forced over the warming element and funnelled into the plastic hood where the infant is kept. The infant's thermal environment is regulated by controlling the air temperature within the hood or by servo-controlling the heating device to the infant's skin temperature (34). These devices intend on reducing evaporative and convective heat loss. These two devices have been extensively studied yet no clear consensus exists with regards to which one confers the greatest advantage during intensive care (35). Nevertheless, despite their heterogeneous usage, current trends in NICU practice across North America and Europe are to employ Radiant Warmers in order to thermally support neonates. This can be attributed to the simple fact that radiant warmers allow for easy access to the patient so that nurses may administer care without heavily impacting the neonate's environment (9).



Figure 4. NICU Incubator



Figure 5. NICU Radiant Warmer

Heat Exchange

The human heat balance equation has two distinct parts, one referring to metabolic heat production [See section 2.3] and the other human/environmental heat exchange. Heat exchange avenues [i.e. Radiation, Convection, Conduction and Evaporation] are essential to maintain a stable core temperature as they represent the only way for the body to compensate for the rate of metabolic heat production within the body. A failure to balance the rate of heat lost to the external environment with the rate at which heat produced from metabolism leads to a change in body heat content. Conversely, these same heat loss mechanisms can predispose the body to excessive heat loss relative to heat production, which may lead to the onset of hypothermia. As such it is important to consider each of these 4 distinct heat exchange avenues in order to properly assess a given thermal environment.

Dry Heat Transfer

Dry heat transfer is the main collective pathway of heat exchange in neonates and refers to the combination of convective, conductive and radiative heat exchange avenues between the body and external environment (6). However, during neonatal intensive care, in-patients are generally provided with an external heat source, meaning that it is rare that there is a loss in all three of these avenues. Nevertheless, they are often considered as one entity. For example, a key study by Elabbassi *et al.* found that the rate of total dry heat loss from the skin was directly proportional to the body surface area-to-mass ratio to in neonates (29). This relation was established by using mannequin models of two LBW infants one weighing 1200 grams and 900 grams respectively and assessing their relative dry heat exchanges under various thermal conditions. Logically, the results confirm that

PT and LBW newborns, having larger surface area-to-mass ratios than FT infants, are particularly vulnerable to the risk of hypothermia via dry heat exchange. Ginalski *et al.* found similar results while studying mannequin nursed under the same conditions but in incubators rather than radiant warmers (36). In spite of this, it is important to note that both these findings were conducted under artificial conditions while using computational models to calculate various heat exchange pathways. Although both these authors claim that their findings can be generalized to treatment in the NICU, no definite conclusions can be drawn until heat exchanges in neonates are assessed *in vivo* with active physiological control systems and the true biophysical characteristics.

Conductive Heat Transfer

Conductive heat loss [K], defined as transfer of heat by direct contact of particles of solid matter, has widely been regarded as an insignificant factor in neonatal intensive care. It has been shown to have a relatively small contribution to total heat exchange in infants undergoing intensive care (37). In fact, Tourneaux *et al.* described that, quantitatively, conductive heat transfer is the least important factor in heat balance and only represents roughly 1-3% total heat loss in neonates (32). This can be attributed to the fact that the only physical surface that neonates are in direct contact with is the mattress upon which they sleep. Furthermore, the body surface area in direct contact with the mattress only represents ~10 to 15% of the infant's total body surface area (38). As such, other avenues of heat transfer are considered more important in the scope to thermal management strategies. However, it is interesting to note that Topper *et al.* reported that by implementing the use of a heated mattress they were able to markedly reduce temperature gradients throughout the body in very low birth weight infants kept under

radiant warmers (25). Furthermore, when a heated pad was used in parallel with a radiant warmer, the wattage of the radiant warmer over a given period of time was reduced. In spite of this, by considering Topper's findings from a heat balance perspective, it is entirely logical that the radiant heat requirement to maintain heat balance is reduced by creating a positive conductive heat transfer in the infants. It would be pertinent to explore whether the provision of an external conductive heat load would provide a better means of maintaining heat balance in neonates.

Radiative Heat Transfer


Heat loss through radiation [R] is related to the temperature of the surfaces surrounding, but not in direct contact, with the infant. The newborn infant emits heat energy in the form of infrared electromagnetic waves (32). The loss or gain of this radiant energy is proportional to the temperature difference between the skin and the radiating bodies; heat may be lost from the infant's body to a nearby cold wall or window for example (20, 32). It has been shown that radiative heat exchange is an important heat loss pathway in infants (38), thus, many newborns are kept under radiant warmers, which invoke a gain in radiant heat (38, 43). As such, rather than being enclosed within a fixed environment such as in an incubator, they are exposed to the ambient environment within the NICU. Therefore, neonates experience greater levels of evaporative, and convective heat loss in addition to radiant heat gain (40). In essence, the role of radiant heat provision is to compensate for convective and evaporative heat loss avenues. Baumgart (1985) first investigated the partitioning of heat losses and gain in neonates under radiant warmers (39). By quantifying each heat exchange variable at different servo-control temperatures, he found that despite the steady flux of radiant heat to the infants, there

existed a disparity between the rate of radiant heat provided by the radiant warmer and the amount of radiant required to attain heat balance (39). Though the data collected during this study indicates that infants are found to be 'heat balanced' over time, the servo-control system appeared to actively promote a sinusoidal pattern of change in body heat content. Since it has been well established that variations in core temperature lead to negative clinical outcomes, it is logical to assume that by mitigating any form of core temperature change, one would improve the environment under which the infant is kept. Therefore, despite how minimal the core temperature variations under radiant warmers may be, any exposure to cold strain could adversely affect the health of the infant.

Since abdominal skin temperature serves as the feedback mechanism, it is reasonable to deduce that there would be a significant time laps between a change in core temperature and a change abdominal skin temperature. This can be attributed to the fact that abdominal skin temperature constitutes a poor proxy for core temperature. Therefore, there is considerable delay between heat loss, via convection and evaporation, before the radiant heater can turn on which causes the change or core temperature. It is important to note that during Baumgart's study, they did not account for the variability of the radiant heat requirement in reference to environmental conditions as well as morphological factors of the individual. This is a particular cause for concern given the fact that these devices are so commonly used in NICUs.

One important notion that Baumgart put forth that is paramount when considering heat balance in neonates nursed under radiant warmers is the discrepancy between the rate of radiant heat required to attain heat balance (R_{req}) and the amount of radiant heat actually provided by the radiant heat lamp (R_{prov}). Theoretically, these two variables

should be equal if the newborn is to have a stable core temperature throughout intensive care. In a situation where one would exceed the other, there would be a resultant change in body heat content that would subsequently alter core temperature. That is, if $R_{req} > R_{prov}$, core temperature decreases; and if $R_{prov} > R_{req}$, core temperature increases. By relying on the heat balance equation, quantifying each relevant variable and isolating the radiant heat component, it is possible to define any resulting difference between R_{req} and R_{prov} [Figure6]. If one is greater than the other, there a concomitant rise or fall in core temperature. Ideally, a radiant warmer that provides a thermoneutral environment for a newborn must provide the exact rate of radiant heat required for the infant in order maintain heat balance.

$$R_{Req} = K \pm C + E - M \quad W/m^2$$


$$\rightarrow R_{Req} = R_{Prov} \quad \therefore S=0 \quad W/m^2$$

Figure 6.Calculating Radiant Heat Required

While Baumgart's findings indicate that, over time, the infants had experienced an equal rate of radiant heat flux [R_{prov}] in reference to the rate of radiant heat required to achieve heat balance [R_{req}], this was only the case on a long term basis. Looking at the data within short timeframe, it is evident that this system allows for the body to experience transient positive and negative heat storage that could potentially go beyond tolerable limits leading to hypo/hyperthermia. By actively heating up and cooling down the infants, the radiant warmer induces thermal strain that could negatively affect clinical outcomes. Though no information currently exists regarding specific clinical outcomes relating to infants nursed under radiant warmers (40), it is reasonable to assume that any deviation from the body's thermoneutral range, no matter how small, could potentially

affect the propensity for poor health (slowed growth rate or even increased risk of morbidity). Ideally, these core temperature variations should be as small in magnitude as possible (35) and as such, it would be favourable to investigate whether the provision of a constant radiant heat load that precisely contrasts the level of radiant heat needed to attain heat balance would improve this method of thermal management.

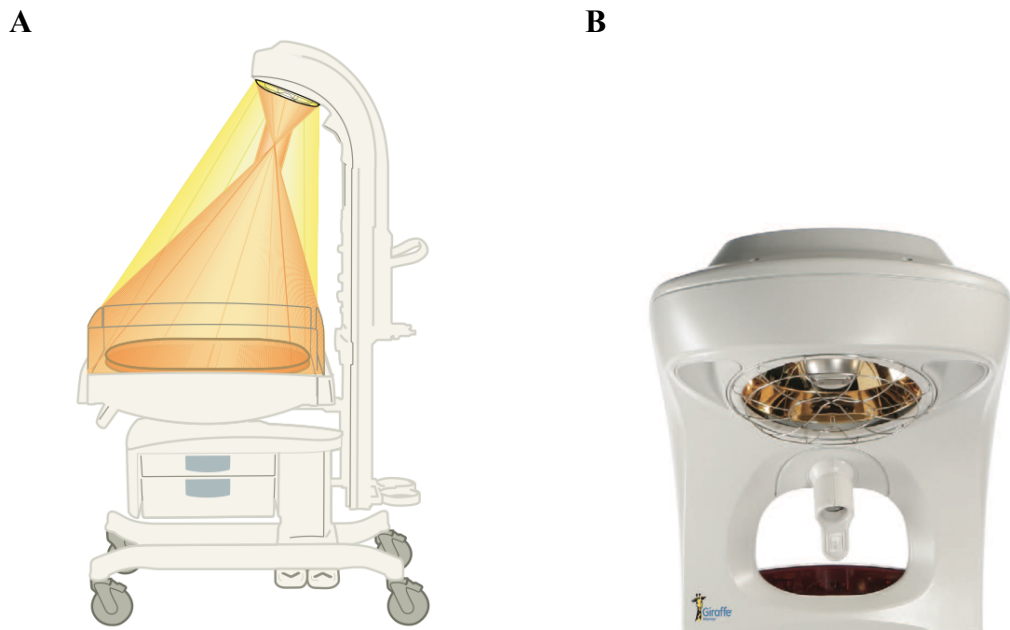


Fig. 7.(A) Radiation Emission Profile of the Giraffe Radiant Warmer and (B) Radiant Heat Lamp.

Evaporative Heat Loss

Evaporative heat loss [E] is defined as heat transfer from the body to the environment through evaporation of water (32). When considering human heat balance, it is important to note that it is the only heat exchange avenue that is exclusively negative, *i.e.* it is impossible to gain heat by evaporation, only lose it. During evaporation, water is converted from a liquid to a gas, causing approximately 2260 Joules of heat to be lost for every gram of water evaporated from the body (20). This transfer can either be accomplished through transepidermal water loss [TEWL] or evaporation by respiration

(32). It has been shown that total evaporative heat transfer is the main mechanism of heat dissipation from the body in infants kept under radiant warmers (26, 44).

Considering neonates' thin epidermis and high surface area-to-mass ratio it is not surprising to note that evaporative heat transfer is significant factor in total heat loss. As such, evaporative heat loss has been extensively researched in an NICU setting. Wheldon *et al.* investigated metabolic heat production in PT and LBW infants and the evaporative heat losses from the skin and found that for PT infants with less than 30 weeks gestation, heat losses due to evaporation equated to roughly 30% of total heat loss (45). Although these findings are important, it is essential to understand that the rate of evaporative heat loss is not constant throughout development. Hammarlund *et al.* have conducted several studies on TEWL in neonates and have been able to demonstrate that it is at its peak in the first week of life but gradually decreases thereafter (26). These findings confirmed research by Hey *et al.* indicating that total evaporative heat loss is strongly correlated to postnatal age. In another study, Hammarlund *et al.* found that, when controlling for weight, there was an inverse correlation between IWL through the skin and gestational age relative to total heat loss, meaning the PT infants exhibit higher relative rates of evaporative heat loss when compared to FT infants (26). This data has significant implications for thermal management in the NICU. Given the fact that infants of different gestational and postnatal ages exhibit different rates of total evaporative heat loss, no one method of thermal management could adequately maintain a thermoneutral environment for these infants.

Finally, one of the most important factors when considering evaporative heat exchange is the fact that the rate of evaporative heat loss varies depending on ambient

humidity as well as air velocity. As the relationship between evaporative heat loss via TEWL and humidity at a fixed air velocity is an inversely linear one, evaporative losses can be reduced with the provision of high-level relative humidity. However, evidence has yet to emerge in relation to the optimal level of humidity over time without limiting epidermal development. Evaporative heat loss is also directly proportional to the velocity of air moving over the body. This convective component is important to consider in infants exposed to the ambient environment since any change in air circulation will not only affect convective but also evaporative heat loss.

While methods of accurately measuring evaporative heat loss have been clearly established, it is not evident how to mitigate this mode of heat loss in an intensive care setting. The literature seems to point towards incubators as a means to reduce total evaporative heat loss however they seem to be accompanied by a concomitant rise in auxiliary forms of heat loss. Radiant warmers on the other hand make no effort to limit this heat loss avenue and it must therefore be quantified.

Heat Production Mechanisms

Several studies have assessed the metabolic rate of infants kept in an NICU setting as a means of modulating feeding strategies to ensure positive energy balance (6, 30). From a thermoregulatory standpoint, this information is also vital since the goal of neonatal thermal management is to reduce the overall energy expenditure devoted to maintaining a stable core temperature. In PT and LBW neonates, the total metabolic heat produced mirrors the requirements of the body's vital physiological functions; functioning of vital organs, thermoregulation as well as growth and development. In cool environments, the energy used to maintain a constant core body temperature depletes the

energy available for other necessary functions (32). As previously mentioned, with the exception of basal metabolic rate, non-shivering thermogenesis [NST] is the main heat production avenue during cold stress and its role at birth has been well recognized (2, 69). NST represents an increase in heat production derived from an elevation in metabolic rate in the absence of contractile patterns consistent with shivering in the skeletal muscle. The neonate responds to cold stress by initiating an increase in NST in order to compensate for an increased rate of heat loss thus achieving heat balance. Heat production via NST is almost exclusively derived from brown adipose tissue [BAT] metabolism (22, 47, 65, 66). BAT differs morphologically and metabolically from ordinary white adipose tissue in that it contains more mitochondria, numerous fat vacuoles, abundant sympathetic innervations and vascularization (2). However, the most important difference is the tissue's propensity towards heat production through mitochondrial uncoupling via UCP1, a transmembrane protein also known as "thermogenin" (65). By uncoupling the respiratory chain, UCP1 allows for fast substrate oxidation with a low rate of ATP production (66). While many adults still possess this tissue, it has been firmly established that newborn infants have relatively higher levels of BAT (67) and many authors suggest the presence of BAT in neonates to be an adaptive means of compensating for the fact that they cannot produce heat through shivering (64, 69). It is well known that BAT in human is generally deposited after 28 weeks gestation, and principally found around scapulae, kidneys, adrenals, neck and axilla (65). However, studies have demonstrated that the relative quantity and distribution of BAT differs greatly between neonates. Merklin *et al.* found that LBW infants had a proportionally lower relative amount of brown adipose tissue than FT neonates (22).

Given these findings, we can conclude that due to their limited capacity to produce heat, exposure to low environmental temperature in PT and LBW neonates should be avoided as much as possible within the NICU in order to promote positive clinical outcomes.

Bauer *et al.* conducted a prospective study involving 197 (183 PT and 14 FT) neonates on which they measured total metabolic rate by evaluating resting energy expenditure [REE] using indirect calorimetry. They demonstrated that postnatally, there was a gradual increase in REE between the first and the sixth week of life (30). This increase was the greatest in PT infants relative to their weight (48). These findings underscore the importance of thermal management of neonates within an intensive care setting. The fact that so much energy is being devoted to growth and development requires that less be attributed to thermoregulation, a state that could be reached by implementing a thermoneutral environment. In support of this notion, Sinclair suggests that keeping infants in a thermoneutral environment reduces death rate and secondary clinical outcomes such as morbidity in LBW infants in the NICU which can be partially attributed to a high metabolic demand of thermoregulation (34). Sauer *et al.* have defined the thermoneutral environment empirically as ‘an environment which maintains core temperature between 36.7°C and 37.3°C, where core and mean skin temperatures change less than 0.2 – 0.3°C/h’ (87). Whilst these guidelines were established for care within an incubator rather than in a radiant warmer, the fundamental theory still stands. By providing an environment which ensures that core and skin temperatures do not fluctuate beyond a fixed range and at a slow rate within a fixed time frame, one would effectively be mitigating the onset of undue thermal strain. Unfortunately, due to the circumstantial nature of the data and the ethical boundaries within this setting, no studies have been

conducted on the direct effect on the thermal environment on growth rates in the NICU. In light of neonates' limited capacity to produce heat we can conclude that by keeping infants in a thermoneutral environment, the metabolic heat requirements for thermoregulation would be markedly reduced and there would potentially be a concomitant reduction in negative clinical outcomes.

Despite the relative validity of evaluating total metabolic rate in neonates, in order to adequately assess the metabolic implications of maintaining normothermia, it is important to couple this information with the heat loss components of the human heat balance equation. By determining total heat production and comparing it with the net exchange to the environment, we would be able to critically assess a neonate's thermal status in reference to their rate of heat storage in order to delineate the dynamics of heat balance using current thermal management techniques. This information could then be used in order to modify thermal management strategies accordingly. There is clearly a need for a more exhaustive, partitioned audit of metabolic heat production in neonates that could be used to precisely orient thermal management techniques.

Implications for Future Research

In spite of the reduction in the incidence of neonatal hypothermia over the past 20 years (3) there exists much room for improvement. As we've described throughout this review, the association between survival of a newborn and the thermal environment has been well recognized. Researchers and clinicians know that a thermoneutral environment is the most effective way to mitigate the risk hypothermia in infants kept in an NICU. However, it is still unclear how to maintain a thermoneutral environment throughout a patient's stay. Given the inter-individual variability that exists between NICU patients

and the variety of thermal management practices, it seems virtually impossible to define one standard method. Recent findings suggest that the evaluation of heat exchanges between the body of the neonate and the environment would allow for a more precise method of establishing the appropriate thermal parameters for a given child, however very few studies have done so *in vivo*.

Most hospitals currently employ the use of radiant warmers in its NICUs to care for many of its PT and LBW neonates since they allow for closer monitoring of in-patients. While the effectiveness of these devices has been heavily documented in literature it is still ambiguous whether they provide adequate thermal support for the patients. The fact that the infant is exposed to the external environment raises some level of concern in this regard. It has been shown that evaporative and convective heat loss is high in infants kept under radiant warmers. Although the provision of radiant heat has been shown to compensate largely for these heat loss avenues, they are never constant throughout the newborns tenure in the NICU. The effect of variations in the thermal environment could also be exacerbated by two factors rarely considered in literature, the external site used for core temperature estimation that triggers the feedback mechanism and the temperature gradient that exist between various points across the body. Current clinical practice relies on traditional thermometry to assess an infant's thermal status while under a radiant warmer, a method that provides only a partial indicator core temperature and can be highly variable. Silverman and Sinclair both showed that oxygen consumption was lowest when the neonate's temperature had been regulated by servo-controlling the flux of heat to maintain a constant abdominal skin temperature at roughly 36.5°C (5, 34). These findings are logical given the fact that the goal of the radiant

warmer is to maintain a stable body temperature rather than air temperature, however they do not take into account the validity of the measurement site as a mean to accurately assess core temperature. In support of this, Seguin et al. reported that abdominal skin temperature was not an accurate surrogate for true core temperature in neonates kept under radiant warmers (56). In their study, the mean error between abdominal and oesophageal temperature over the course of the recording period was highly variable, meaning that changes in local skin temperature that would prompt changes in radiant heat output can occur independently of changes in true core temperature. This implies that while abdominal skin temperature was a relatively accurate proxy for a more reliable 'core' temperature in very low birthweight neonates, the mean error could increase the risk of passive over/under-heating of the infant. These findings are surprising since this study only included very low birthweight neonates (i.e. <1000 grams), a population that has a very low mean error between oesophageal and abdominal temperature due to their body morphology. Preliminary data part of an ongoing study (85) demonstrates that the mean error between abdominal skin temperature in infants increases with age and can be as high as 0.9°C by 24 weeks of age. The question remains, are radiant warmers providing adequate thermal support for neonates? More specifically is the rate of radiant heat provision equal to the required rate of radiant heat for heat balance and do morphological factors correlate to these heat exchange variables?

III. RESEARCH PROJECT

Purpose

This study aims to critically assess the thermal environment of neonates in an intensive care setting kept under servo-controlled radiant warmers. This will be achieved *in vivo* with a model of *Partitional Calorimetry* that measures specific heat exchange avenues between the infant's body and the external environment. More specifically, we plan to focus on the radiant heat component of the human heat balance equation in order to define whether a disparity exists over time between the rate of radiant heat provided to the patient and the rate of radiant heat required to attain heat balance.

Study Objectives:

Primary Objective:

- Quantify the rate of radiant heat provided by the radiant warmer over time and compare it to the rate of radiant heat required to attain heat balance in infants nursed under radiant warmers during intensive care.

Secondary Objectives:

- Compare axillary temperature, used in the servo-control feedback loop that regulates radiant warmer heat flux, to core temperature as measured by rectal temperature.
- Determine whether a thermoneutral environment is being provided to patients nursed under radiant warmer according to Sauer et al.'s definition of the thermoneutral environment (87).

- Determine how the rate of radiant heat required and the amount of radiant heat provided are influenced by various morphological factors such as gestational age, weight, surface area-to-mass ratio and skin thickness.

Rationale

In the majority of cases, infants kept under radiant warmers in the NICU do not experience hypo/hyperthermic episodes (39), it is therefore reasonable to assume that the servo-control system used as a feedback mechanism for the flux of radiant heat provided to the infant by the radiant warmer ensures that core temperature does not change drastically over time. However, within a given time frame, it is unclear to what magnitude 'core' temperature fluctuates [Figure 8] since an axillary skin temperature sensor is used as a proxy for core temperature, a thermometric technique which has been shown to exhibit a clinically significant level of mean error with a reference core temperature in newborn infants (56). The discrepancy between core temperature and abdominal skin temperature could predispose an infant to passive over/under heating which would lead to a sinusoidal imbalance between the amount of heat gain and the amount of heat lost to the external environment subsequently leading to changes in core temperature. In environmental conditions where infants are forced to actively maintain core temperature due to cold/heat stress, a given amount of energy is devoted to thermoregulatory responses. This could deplete their energy stores that could otherwise be used for other important physiological processes and likely delay their rate of recovery. Due the fact that core temperature changes have been shown to lead to negative clinical outcomes (12-16), we can infer that even the smallest variations beyond the

body's tolerable range could affect a newborn infant's health. While these changes in core temperature may be minimal, it is advantageous to mitigate them as much as possible. Therefore, there is a need for assessing the human/environmental heat exchange of these infants by auditing specific heat exchange avenues and determine whether the external heat load provided by the radiant warmer equates the rate of radiant heat required for the patient to attain heat balance over time.

Hypotheses

1. The rate of radiant heat provided by the radiant warmer and the rate of radiant heat required to attain heat balance in the same participant are equal over a prolonged time period (105 min.) due to the feedback mechanism used to control the flux of radiant heat from the warmer (35). However, a minute-by-minute analysis of these two components would likely expose a chronic but transient discrepancy that would actively induce a sinusoidal pattern of deep core temperature variation [Figure 8].
2. Axillary temperature used by the radiant warmer does not significantly correlate with rectal temperature.
3. By virtue of large fluctuations in both core and skin temperatures, a thermoneutral environment is not being provided to patients nursed under radiant warmers.
4. Morphological factors such as surface area-to-mass ratio, skin thickness and gestational age are positively correlated with the rate of radiant heat required to maintain heat balance.

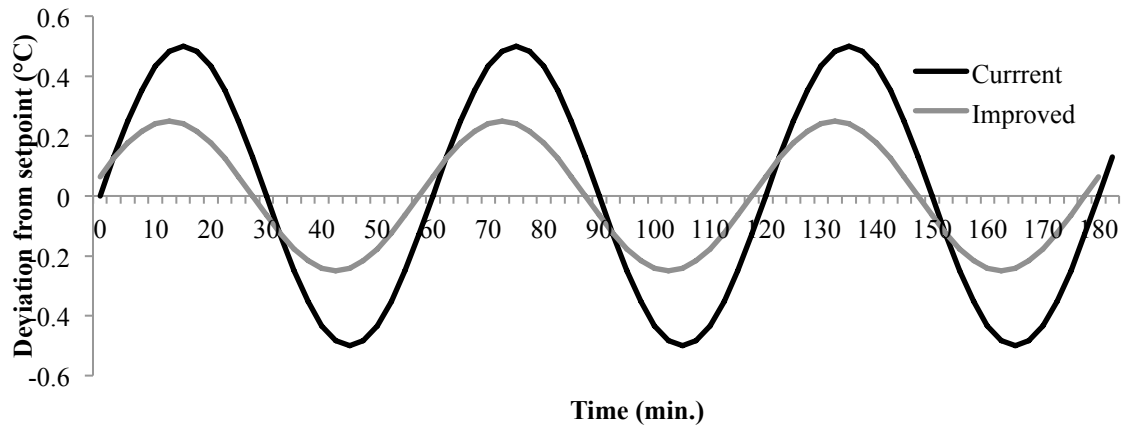


Figure 8. Theoretical conceptualization of ‘core’ temperature variation during neonatal intensive care under a servo-controlled radiant warmer; current versus ideal conditions.

Relevance

Critically assessing the thermal environment of newborns nursed within an intensive care setting using a theoretical approach based on heat exchanges rather than just temperature will allow us to determine whether a thermoneutral environment is actually being provided to patients. In addition, this project will yield essential information regarding clinical practice pertaining to thermal management that could contribute to significant improvements to the methodology used in order to maintain a thermoneutral environment. This project will therefore contribute to further expanding our knowledge of thermal management within the NICU using radiant warmers.

Methodology

**NB: The experimental methodology of the current project is described in detail within the “Methods” section of Part Two of this document.*

PART TWO: RESULTS OF THE THESIS

Quantifying heat balance components in neonates nursed under radiant warmers in intensive care

Yannick Molgat-Seon¹, Thierry Daboval^{2,3,5}, Shirley Chou^{2,4,5}, and Ollie Jay^{1,2}✉

¹Thermal Ergonomics Laboratory, Faculty of Health Sciences, University of Ottawa, Canada

²Childrens Hospital of Eastern Ontario Research Institute, Ottawa, Canada

³Division of Neonatology, Children's Hospital of Eastern Ontario, Ottawa, Canada

⁴Dept. of General Surgery, Children's Hospital of Eastern Ontario, Ottawa, Canada

⁵Faculty of Medicine, University of Ottawa, Canada

ABSTRACT

Neonatal intensive care units use radiant warmers (RW) to maintain stable body temperatures in many newborns. This study examined; 1) whether the rate of radiant heat required for heat balance (R_{req}) is equal to the rate of radiant heat provided by the RW (R_{prov}), 2) whether a thermoneutral environment was being provided by the RW, 3) the correlation between rectal temperature (T_{re}) and axilla temperature used to control RW heat output (T_{feedback}), and 4) the magnitude to which care and skin temperatures fluctuate over time. A systematic evaluation of time-dependent changes in heat balance components was conducted in 10 newborns (mass: 2829 ± 636 g; age: 9.2 ± 11.0 days; BSA: 0.19 ± 0.03 m²) nursed under RW. Metabolic rate, evaporative heat loss, convective and conductive heat flow, T_{re} and mean skin temperature (T_{sk}) were measured continuously for 105 min. The rate of body heat storage (S) was calculated using a two-compartment model of 'core' (T_{re}) and 'shell' (T_{sk}) temperatures. Mean R_{prov} (1.56 ± 2.41 W) and R_{req} (1.67 ± 2.18 W) were not significantly different ($P=0.56$). However, while the resultant mean change in body heat content after 105 min was low ($+0.46 \pm 2.79$ kJ) and not significantly different from zero ($P>0.05$), an acute time-dependent change in body heat storage was evidenced by a mean positive heat storage component of $+6.64 \pm 2.98$ kJ and a mean negative heat storage component of -6.17 ± 2.64 kJ. Accordingly, the mean difference between maximum and minimum values for T_{re} and T_{sk} were $0.71 \pm 0.37^\circ\text{C}$ and $2.18 \pm 0.81^\circ\text{C}$ respectively. On average, there was no significant difference between T_{re} and T_{feedback} ($p=0.79$). However, T_{feedback} did not significantly correlate with changes in T_{re} overall ($r=0.21$, $P=0.581$). In conclusion, while RW maintain a stable core temperature over a prolonged period, they induce acute bouts of heat imbalance, a fact which may be exacerbated by the poor correlation between T_{feedback} core body temperature.

INTRODUCTION

For newborns admitted to the Neonatal Intensive Care Unit (NICU), providing an optimal thermal environment is a priority to ensure survival, recovery and growth (1-4). By virtue of their immature thermoregulatory system and a morphological susceptibility to excessive heat dissipation, newborn infants are predisposed to deleterious reductions in core body temperature (5-11). Providing a thermoneutral environment (TNE) has been described as the most effective approach to neonatal thermal management (12). Sauer et al. defined the TNE empirically as an environment which maintains core temperature between 36.7°C and 37.3°C, where core and mean skin temperatures change less than 0.2 to 0.3°C/h (13). The maintenance of a TNE can be achieved by providing sufficient thermal support to ensure steady-state body temperatures by way of passive heat exchange rather than active response (14, 15). While the concept of providing a TNE succeeds in theory, it remains a challenge for patients nursed under radiant warmers (RW) even in modern NICUs (16, 17).

Radiant Warmers are open beds with a radiant heat source placed above a neonate to provide external thermal support while allowing nurses ease of access and visibility to the patient (18). The radiant heat source output is servo-controlled by a single local skin temperature measurement over the axilla. While these devices have been shown to contribute to maintaining rectal temperature stable in term newborns (19), many authors suggest that there is still much room for improvement (17, 20, 21).

First, a feedback mechanism relying on a single measure of skin temperature increases the risk for passive over/under-heating. Studies have shown that axillary temperature, used in the RW negative feedback loop, does not accurately reflect core

body temperature as measured in the rectum (T_{re}) in term newborns (22, 23, 24). Secondly, the RW does not account for the rate of radiant heat needed for heat balance, but rather responds to acute changes in local skin temperature regulated around a set-point local skin temperature (25, 26). This acute variation in radiant heat output likely induces transient periods of heat storage and heat debt that are approximately equal over time but lead to oscillations in core and skin temperature that exceed those defining a TNE. Since even small changes in the thermal environment have been shown to have a significant effect on neonatal mortality (11), it is clear that any fluctuations beyond a tolerable range should be avoided. Lastly, most tertiary NICUs care for a large continuum of neonates under RWs, ranging from very-low birthweight infants (<1000 grams) to term newborns (>2500 grams at birth). Biophysical characteristics such as body surface area, weight and length all influence human-environment heat exchange (1). Given the fact that the morphological variation within this population is large, it is likely that the radiant heat required to maintain heat balance varies between patients. Indeed, some patients may need no radiant heat support due their physical characteristics.

While some contemporary studies have conducted heat balance investigations of the thermal environment of newborns under RWs (27, 46), few have been conducted *in vivo* (28, 29) and, to our knowledge, no study has quantified time dependent changes in heat balance components. Indeed, it has been recently stated that a more rigorous evaluation of heat exchanges affecting the body in neonates is needed to allow a more precise method of establishing the appropriate thermal parameters for a given child (21).

The present study concurrently assessed neonatal heat balance and thermal status using partitional calorimetry and thermometry in NICU patients nursed under RWs

throughout a 105 minute period. It was hypothesized that; i) while the mean rate of radiant heat provided by the RW (R_{prov}) is similar to the mean rate of radiant heat required to attain heat balance (R_{req}) over a prolonged period (i.e. 105 min), alternating bouts of systematic positive and negative heat storage occur that are significantly different from zero; ii) the resultant oscillations in core and regional skin temperatures across the body exceed those defining a TNE; iii) axillary skin temperature ($T_{feedback}$) used in the servo-control loop regulating the radiant warmer does not correlate with rectal temperature (T_{re}), and iv) an individual's R_{req} can be determined using their morphological characteristics.

METHODS

Participants

Following approval by the Research Ethics Board of the Children's Hospital of Eastern Ontario Research Institute, 10 neonates (body mass: 2829 ± 636 g; gestational age: 35.9 ± 3.1 weeks; postnatal age: 9.2 ± 11.0 days; body surface area: 0.19 ± 0.03 m²) admitted to a tertiary level Neonatal Intensive Care Unit (NICU) were included in the study. Subjects were recruited from the NICU at the Children's Hospital of Eastern Ontario in Ottawa, Canada, where written and informed consent was obtained from the legal guardians of each participating patient. Newborn infants in the NICU were deemed eligible for the study if they were between 0 and 30 days of age, nursed under a servo-controlled radiant warmer (Giraffe Warmer, GE Healthcare, Helsinki, Finland), and mechanically ventilated using a standard infant ventilator. Patients were excluded if they were hemodynamically unstable, on high-frequency ventilation, considered immunocompromised, had any medical conditions that had confounding thermoregulatory effects (e.g. hypoxic-ischemic encephalopathy, malignant hyperthermia, neonatal sepsis etc.) or had malformations that precluded the placement or insertion of any temperature probe or skin temperature sensor (e.g. gastroschisis, peripheral skin lesions etc.).

Instrumentation

Thermometry & Heat Flow

Rectal temperature (T_{re}) was measured using a pediatric general purpose thermistor probe (400 Series, Model# ER400-9, Smiths Medical, Dublin, OH, USA)

inserted to a minimum depth of 3 cm past the anal sphincter, as previously reported (30, 31). Skin temperature (T_{sk}) was measured at 7 standardized anatomical sites over the right side of the body (foot, thigh, abdomen, chest, back, arm and forehead) using adhesive thermistor probes (400 Series, Model# STS-400, Smiths Medical, Dublin, OH, USA). The local rate of conductive heat flow of the back (K_{back}) was measured using 0.3 mm diameter T-type (copper/constantan) thermocouple integrated into a heat-flow sensor (Concept Engineering, Old Saybrook, CT, USA). This sensor was attached with surgical tape routinely used within the NICU (Transpore, 3M, St. Paul, MN, USA). Servo-control temperature ($T_{feedback}$), as measured by axilla temperature and radiant output from the warmer (%) will be recorded for every minute directly for the RW (Giraffe Warmer, GE Healthcare, Helsinki, Finland).

Body Mass

Before the start of data collection, patients were placed on a standard mattress under a weighing platform integrated into the RW with a precision of 0.1 g (MS12001L, Mettler Toledo, Columbus, OH, USA). This device was designed to bear no alteration to standard care setup all the while tracking mass change over time without interfering with the functioning of the RW. Infants remained on the mattress under platform for the duration of each experimental trial. After controlling for the addition of intravenous fluids, secretion of urine/feces and metabolic weight loss from CO_2 , any further mass change was attributed to evaporative water loss (EWL). Thus, each gram of body mass lost represents a rate of heat loss equating to the latent heat of vaporization of water of 2430 J/g (32).

Ventilatory Parameters

Infants were intubated with an endotracheal tube and mechanically ventilated using a standard infant ventilator (DrägerBabylogVN500, Dräger Medical, Lübeck, Germany) which measured and recorded respiratory rate (RR), Tidal Volume (V_T), Minute ventilation (V_e), Fraction of Inspired Oxygen (F_iO_2), Fraction of Inspired carbon dioxide (F_iCO_2) and, the partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$) every minute.

Environmental Parameters

Ambient air temperature (T_a) and relative humidity (RH) were measured with a level of precision of $\pm 0.5^\circ C$ and $\pm 5\%$ RH using a USB Temperature and Humidity monitor (DIGI, Minnetonka, MN, USA). Air velocity (v) was measured using a multi-directional Hot Wire Anemometer (Model HHH2005HW, Omega Canada, Laval, QC). Barometric pressure was measured by the infant ventilator (DrägerBabylogVN500, Dräger Medical, Lübeck, Germany).

Calculations

Body surface area (BSA) in m^2 , was calculated based on infant body mass in kg, and length in cm, using Haycock's equation (33):

$$BSA = [(mass^{0.5378}) * (length^{0.3964})] * 0.024265 \dots \dots \dots m^2 \dots \dots \dots (1)$$

Mean skin temperature (T_{sk}) in degrees Celsius, was calculated from the local skin temperatures and weighted according to the surface area of each segment (head 21%, trunk 32%, arm 17%, leg 26% and foot 4%) (34, 35). As such, temperature of the head was measured according to forehead temperature, temperature of the trunk was measured by the average between back, chest and abdomen temperature, leg temperature was measured on the thigh and foot tempera on the forefoot, all in degrees Celsius.

Human Heat Balance

A conceptual model of human heat balance was employed including metabolic energy expenditure (M) and the separate heat transfer avenues of conduction (K), radiation (R), convection (C), and evaporation (E), all in kJ/min (1, 15). Participants did not perform any external work (W), thus it was considered negligible. Any resultant imbalance in the equation is characterized as body heat storage (S):

$$M = K \pm C \pm R - E \pm S \dots\dots\dots kJ/min \dots\dots\dots(2)$$

$$S = M \pm K \pm C \pm R - E \dots\dots\dots kJ/min \dots\dots\dots(3)$$

Metabolic energy expenditure (M) was calculated using indirect calorimetry. Carbon dioxide production was measured using the partial pressure of end-tidal CO₂($P_{ET}CO_2$) in mmHg, the partial pressure of inspired CO₂ (P_iCO_2) in mmHg, minute ventilation (V_E) in L/min and barometric pressure (P_{Bar}) in mmHg, according to the following equation:

$$VCO_2 = V_E [(P_iCO_2 - P_{ET}CO_2) / P_{Bar}] \dots\dots\dots L/min \dots\dots\dots(4)$$

Oxygen consumption in L/min, was then estimated based on the relation between VO_2 and VCO_2 by assuming an RER of 1.0 as previously reported in parenterally fed, ventilator dependent newborns under RW (36, 37).

$$VO_2 = VCO_2 * RER. \dots\dots\dots L/min. \dots\dots\dots (5)$$

Metabolic energy expenditure (M) in kJ/min, was subsequently derived using the following equation:

$$M = [(VO_2 * [(RER - 0.7 / 0.3) * E_C] + [(1 - RER / 0.3) * E_F]). \dots\dots kJ/min. \dots\dots\dots (6)$$

Where: E_C is the caloric equivalent per liter of oxygen for the oxidation of carbohydrates (21.13 kJ), and E_F is the caloric equivalent per liter of oxygen for the oxidation of fat (19.62 kJ).

Convective heat transfer (C) was calculated using the convective heat transfer coefficient, ($h_c = 3.1 \text{ W m}^{-2} \text{ K}^{-1}$ for air velocities less than 0.2 m/s), the difference between the air (T_a) and mean skin (T_{sk}) temperatures in degrees Celsius, as well as the fraction of body surface area available for convective heat transfer (A_c) in m^2 :

$$C = \{ [h_c (T_{sk} - T_{air}) * A_c] / 1000 \} * 60. \dots\dots\dots kJ/min. \dots\dots\dots (7)$$

Conductive heat transfer (K) depends on the fraction of body surface area in contact with the mattress (A_k) in m^2 , and the rate of local heat flow between the back and the mattress (K_{back}) in W/m^2 . A_k was estimated using a percentage of body surface area previously reported (7.3% of total body surface area) (38). Hence:

$$K = [(A_k K_{back}) / 1000] * 60 \dots \dots \dots kJ/min. \dots \dots \dots (8)$$

Evaporative heat loss (E) was estimated using the infant's mass change over time in grams, after adjusting for the mass of intravenous fluids. Mass from intravenous fluids was obtained by dividing the total mass of the solution by its total volume and multiplying the result by the rate of infusion and the duration of the trial. Hence:

$$E = [(\Delta mass / t) * 2.430] / 1000 * 60 \dots \dots \dots kJ/min \dots \dots \dots (9)$$

Where: $\Delta mass$ represents the change in adjusted infant body mass in kg over 105 minutes.

The rate of body heat storage (S) was calculated every 5 minutes using a two-compartment model of 'core' (T_{re}) and 'shell' (T_{sk}) temperatures in degrees Celsius as previously reported (38, 39).

$$S = [(0.6 \Delta T_{re} + 0.4 \Delta T_{sk}) * mass] * C_{sp} \dots \dots \dots kJ/min. \dots \dots \dots (10)$$

Where: ΔT_{sk} and ΔT_{re} indicate the respective changes in mean skin temperature and rectal temperature over a 5 minute time frame in degrees Celsius, mass represents infant body mass in kg, and C_{sp} (3.494 kJ/°C/kg) represents the specific heat capacity of human tissue (38).

The rate of radiant heat provided to the patient (R_{prov}) and the rate of radiant heat required to attain heat balance (R_{req}) in kJ/min, were calculated by isolating R in the conceptual heat balance equation (equation). The calculation for R_{prov} incorporated S, calculated using equation 10, in order to account for any changes in body heat content. R_{req} was calculated under the assumption of an S of zero, where heat balance was attained. Hence:

$$R_{prov} = M - E \pm (K \pm C) \pm S \dots \dots \dots .kJ/min \dots \dots \dots (11)$$

$$R_{req} = M - E \pm (K \pm C) \dots \dots \dots .kJ/min. \dots \dots \dots (12)$$

Experimental Protocol

Before beginning testing, anthropometric data (mass, length, age, gestational age and sex) were recorded by hand from the participant’s chart on a standardized case report form. Nursing staff then placed the infant onto the weighting platform integrated into the servo-controlled RW. Skin temperature sensors were then placed on 7 standardized anatomical sites previously described and a rectal thermometer was then inserted by a member of the nursing staff. Experimental trials lasted a total of 105 minutes during which the patient was left undisturbed. All data were collected using a National

Instruments data acquisition module (model NI cDAQ-9172) at a sampling rate of 1 Hz. Data were simultaneously displayed and recorded in spreadsheet format on a personal computer (Dell Inspiron 545) with LabVIEW 2009 software (Version 8.6.1, National Instruments, Austin, TX).

Statistical Analysis

All data are presented as means \pm standard deviations (SD). Paired sample t-tests were used to compare R_{req} and R_{prov} , as well as T_{re} and T_{feedback} . 95% confidence intervals were calculated for S and observing whether these intervals included zero is equivalent to testing to the null hypothesis that S does not differ significantly from zero at the 0.05 significance level. For each subject, positive and negative components of S were separated and summed in order to define the average rates of positive and negative heat storage respectively. Thermometric measurements were then divided into three conditions according to RW feedback temperature (T_{feedback}); the “below set-point” condition was defined by a T_{feedback} of -0.2°C or less relative to baseline servo-control temperature of 36.5°C , the “set-point” condition was defined by a T_{feedback} of between -0.2 and $+0.2^{\circ}\text{C}$ relative to baseline, and the “above set-point” condition was defined by a T_{feedback} temperature of $+0.2^{\circ}\text{C}$ or greater relative to baseline. The conditions were selected in order to represent both side null zone set-point of the RW. Simple regression analyses were performed between measures of T_{re} and T_{feedback} for each condition (below set-point, set-point and above set-point). Paired sample t-tests were used to compare measures of T_{sk} and T_{re} between these conditions. Simple regression analyses were performed between each morphological characteristic and R_{req} . An alpha of 0.05 was set

for all analyses. Statistical analysis was performed using SPSS version 18.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

Heat Balance

The partitioning of heat balance components are presented in Figure 1, and the environmental parameters, in Table 2. Mean evaporative heat loss (E) was 6.60 ± 1.05 W, while dry heat loss by convection (C) was 6.27 ± 0.78 W and via conduction (K), 0.20 ± 0.10 W. The average rate of metabolic heat production (M) was 11.28 ± 2.59 W. In order to attain heat balance (i.e. an average $S = 0$), the difference between the sum of whole body heat loss and M had to be counterbalanced by an R_{req} of 1.67 ± 2.18 W. On average, S (with 95% confidence interval limits in parentheses) was 0.07 ± 0.43 W (+0.33, -0.22 W) and thus, did not differ significantly from zero ($p > 0.05$). As such, R_{prov} was 1.56 ± 2.41 W and R_{req} and R_{prov} were similar on average for the 105 min duration of data collection ($p = 0.56$).

An analysis of changes in S over time for each subject shows that its variability, or rather, the magnitude of heat imbalance is large over this time frame (Figure 2). After 105 minutes, the average positive and negative changes in body heat content were 6.64 ± 2.98 kJ and -6.17 ± 2.64 kJ respectively, while the net cumulative change in body heat content was -0.46 ± 2.79 kJ (Figure 3).

Thermometry

Over the course of the experimental trial, mean T_{re} fluctuated by an average rate of $0.10 \pm 0.10^\circ\text{C}/\text{h}$. Similarly, T_{sk} fluctuated to the order of $0.36 \pm 0.35^\circ\text{C}/\text{h}$. However, it was observed that core and skin temperatures varied in a sinusoidal pattern. As such, the average peak rate of change in T_{re} was $1.85 \pm 1.87^\circ\text{C}/\text{h}$ and the average positive and

negative rates of change were $0.82\pm 0.41^{\circ}\text{C/h}$ and $-1.00\pm 0.49^{\circ}\text{C/h}$ respectively. The average peak rate of change in T_{sk} was $8.80\pm 9.41^{\circ}\text{C/h}$ and the average positive and negative rates of change were $2.77\pm 0.79^{\circ}\text{C/h}$ and $-4.10\pm 1.88^{\circ}\text{C/h}$ respectively. Figure 6 shows a representative pattern of change in both T_{re} and T_{sk} for one patient.

On average, T_{re} was $36.61\pm 0.50^{\circ}\text{C}$, T_{feedback} was $36.66\pm 0.08^{\circ}\text{C}$ and T_{sk} was $34.68\pm 1.03^{\circ}\text{C}$. Averaged across 105 minutes, there was no significant difference between mean T_{re} and mean T_{feedback} ($p=0.79$). However, T_{feedback} did not significantly correlate with changes in T_{re} overall ($r=0.21, P=0.581$), during the below set-point condition ($r=0.287, P=0.453$), during the set-point condition ($r=0.442, P=0.234$) or during the above set-point condition ($r=0.350, P=0.356$) (Figure 3). Thus, T_{feedback} does not describe the individual variation in T_{re} . As RW heat output changes, the gradient between T_{re} and T_{feedback} was altered from $+0.26\pm 0.46^{\circ}\text{C}$ during the above set-point condition, to $-0.24\pm 0.51^{\circ}\text{C}$ during the below set-point condition. Furthermore, the T_{re} to T_{sk} gradient was $+2.18\pm 1.07^{\circ}\text{C}$ during the above set-point condition and $+1.48\pm 1.02^{\circ}\text{C}$ during the below set-point condition. Furthermore, during the below set-point condition skin temperature was found to be significantly greater than during the above set-point condition at the foot, leg, abdomen, chest, arm and forehead ($p<0.05$) (Figure 5). While these skin temperature sites exhibited large variations according to RW heat output, there was no significant difference in skin temperature of the back and T_{re} ($p>0.05$) (Figure 5).

Biophysical Characteristics

No significant correlations we found between R_{req} and gestational age ($p=0.299$), body surface area ($p=0.394$), weight ($p=0.432$), length ($p=0.442$), postnatal age ($p=0.054$)

or surface area-to-mass ratio ($p=0.509$) (Figure 7). The strongest association with R_{req} was gestational age, which explained 39% of the variation in R_{req} .

DISCUSSION

The continuous assessment of individual heat balance components coupled with thermometric measurements of body temperatures in the present study, allowed for a precise assessment of a neonate's thermal status during standard NICU care under a RW. To date, no study has previously measured time dependent changes in neonatal heat balance under RWs. Previous research has focused on quantifying mechanisms of heat transfer and measuring their relative contribution to whole body heat balance without assessing how they change with time (26, 27, 39-41). The main findings are four-fold; 1) that while RWs facilitate the maintenance of net heat balance over a prolonged period, the acute variation in radiant heat output invoked transient periods of positive and negative heat imbalance; 2) the resultant oscillations in skin temperatures and, to a lesser extent, core temperature exceeded those defining a thermoneutral environment in neonates (13); 3) local skin temperature of the axilla, used to control RW is a very poor surrogate for rectal temperature and 4) the individual variation observed in the rate of radiant heat required for heat balance did not significantly correlate with body morphology.

As indicated by Figure 1, evaporation (E) constituted the largest portion of whole body heat loss at $54.3 \pm 11.8\%$. This observation was consistent with high rates of EWL previously reported in neonates nursed under RWs (42, 43). Convection (C) represented the second largest heat loss avenue and accounted for $44.7 \pm 11.7\%$ of whole body heat loss. In contrast to incubators, RWs increase C substantially by virtue of the fact that they expose the neonate to a lower ambient air temperature (20). In spite of low ambient air velocity ($<0.2\text{m/s}$), the mean gradient between T_{sk} and T_a during our study was

11.3±1.3°C, increasing the drive for convective heat loss. In addition, as the RW heat flux increased, so too did T_{sk} further increasing the rate of convective heat transfer to the ambient environment. Quantitatively, conduction (K) represented the smallest heat loss avenue accounting for the remaining 1.3±0.5%. Endogenous heat production was 11.28±2.59 W based on a mean rate of oxygen consumption of 10.8±3.7 ml/kg/min. These results were similar to those observed in other studies involving term neonates nursed under RWs (29, 47, 48). The mean rate of radiant heat required to attain heat balance (R_{req}) was consequently 1.67±2.18 W. The mean rate of radiant heat provided to the patient (R_{prov}) of 1.56±2.41 W was almost identical to R_{prov} ($P=0.56$). Baumgart (1985) used a similar technique to assess the relation between R_{req} and R_{prov} in a cohort of neonates nursed under RWs and found that 68% of the variation in the rate of radiant heat required for heat balance could be predicted by the rate of radiant heat delivered by the RW (44). However, these data merely report that the rate of radiant heat provision by the RW closely correlated the rate required to attain balance over 90 minutes and did not take into consideration the extent to which body heat storage varied within that time frame. The average rate of body heat storage observed in our study led to a relatively small mean change in body heat content of 0.46±2.79 kJ after 105 minutes which did not differ significantly from zero ($p>0.05$), demonstrating no systematic under- or over-heating. However, while heat balance was attained after 105 minutes, time-dependent changes over this same period of time show large, sinusoidal variations in body heat content. The transient periods of acute negative (-6.2±3.0 kJ), and positive heat storage (+6.9±2.6 kJ) in all participants show that while the body was heat balanced over time, large transient bouts of heat storage occurred. Previous studies have found that during standard care

under a servo-controlled RW, variations in radiant flux density of $\pm 25 \text{ W/m}^2$ can occur within a period of 2 to 3 minutes (25, 26, 41). The fact that the radiant output from the RW fluctuates to such an extent is probably the cause of such transient periods of positive and negative heat storage observed during our study.

Large fluctuations in heat balance, as evidenced by the sinusoidal pattern of change in S suggest that body core and skin temperatures were drastically altered by the flux of radiant heat from the RW. The purpose of the RW is to thermally support neonates as a means of compensating for their propensity towards excessive heat loss. In order to ensure that body temperatures are kept stable, the flux of radiant heat provided must precisely reflect the heat deficit for each patient. The RW relies exclusively on a measure of local skin temperature over the axilla (T_{feedback}) as a source of feedback reflecting this requirement for radiant heat. Previous authors have postulated that axilla temperature does not accurately reflect core temperature (22, 23), suggesting that T_{feedback} may not be the best temperature monitoring site for servo-controlling RW feedback. Our study assessed the relation between average T_{feedback} and average T_{re} and found no significant difference in temperature between these two sites over 105 min ($p=0.794$). However, a simple regression analysis showed that T_{feedback} did not significantly correlate with changes in T_{re} ($r=0.21$, $p=0.581$). This demonstrates that while the mean error between T_{feedback} and T_{re} is small ($0.04 \pm 0.49^\circ\text{C}$), the variability of this error is very high. When the RW increases its output due to a reduction in set-point axillary skin temperature (below set-point condition), the mean error between T_{feedback} and T_{re} was $0.26 \pm 0.46^\circ\text{C}$, whereas when the RW reduces its output due to a increase in set-point axillary skin temperature (above set-point condition), this gradient was inverted to -

0.24±0.51°C. Sauer et al. concluded that a TNE could be defined thermometrically as ‘a state where core temperature is maintained between 36.7 and 37.3°C’ and ‘where core and mean skin temperatures changed less than 0.2 to 0.3°C/h respectively’ (13). Our results demonstrated that on average, rectal temperature was 36.61±0.50°C, just below the threshold of 36.7°C. T_{re} fluctuated at an average rate of 0.10±0.10°C/h, indicating that core temperature was maintained relatively stable under the RW. It should be noted however, that in spite of the low average rate of change in T_{re} the average peak change was 1.85±1.87°C/h and the average positive and negative rates of change were 0.82±0.41°C/h and -1.00±0.49°C/h respectively. Average T_{sk} was 34.68±1.03°C and fluctuated at an average rate of 0.36±0.35°C/h, slightly higher than the maximal rate of change in T_{sk} suggested by Sauer *et al* (13). Similar to changes T_{re} , the average rate of change in T_{sk} is not indicative of the acute bouts of high fluctuation seen in all trials as the average peak change in T_{sk} was 8.80±9.41°C/h and the average positive and negative rates of change were 2.77±0.79°C/h and -4.10±1.88°C/h respectively. Additionally, the mean difference between maximum and minimum values for T_{re} and T_{sk} were 0.71±0.37°C and 2.18±0.81°C respectively, further indicating that there was high variability in both T_{re} and T_{sk} throughout data collection in reference to the thermometric definition of the TNE.

In order to further understand the extent that body temperatures changed under RWs, thermometric measurements were stratified into 3 conditions according to $T_{feedback}$; below set-point ($T_{feedback}$ -0.2°C relative to baseline), set-point ($T_{feedback}$ within±0.2°C of baseline) and above set-point ($T_{feedback}$ +0.2°C relative to baseline). Whilst there were no

significant differences in core or skin temperatures between the below set-point and set-point conditions or the above set-point and set-point conditions ($p>0.05$), skin temperatures of the foot, leg, abdomen, chest, arm and forehead were significantly greater during the above set-point condition relative to the below set-point condition ($p<0.05$) (Figure 5). Foot temperature, having the largest temperature difference between conditions, was $32.07\pm 2.27^{\circ}\text{C}$ during the below set-point condition and $33.21\pm 1.60^{\circ}\text{C}$ during the above set set-point condition, likely due to the distance between the foot and the RW's heat source. In light of these results, it is clear that a TNE is not being provided to neonates under RWs. Fluctuations in both core and skin temperatures of this magnitude are indicative of large bouts of thermal strain which should be mitigated as much as possible. The literature clearly describes that any deviation from the thermal neutral zone increases the risk of complications during NICU care (49).

The current study has shown that while RWs aid in maintaining body temperature stable in neonates in an NICU setting, several concerns regarding their usage still exist. We observed acute variations in whole body thermal status by virtue of large fluctuations in S , T_{sk} and to a lesser extent, T_{re} within 105 min. Paradoxically, these bouts of thermal imbalance appear to be induced by drastic changes in radiant heat output from the RW. As previously shown, $T_{feedback}$ serves as a poor surrogate for core temperature, a fact which may affect the RW's ability to adequately control body temperature in neonates. Moreover, Marks & Gotkiewicz described that the integrity of the servo-control skin temperature probe is easily compromised during regular nursing interventions (46), further signaling that the use of a negative feedback loop relying exclusively on a local

skin temperature in order regulate radiant heat flux from a RW may carry inherent risks of passive over/under-heating.

Future research should focus on determining ways of mitigating acute time-dependent changes in whole body thermal status in neonates under RWs with particular focus on establishing effective methods of reducing large such variations in the rate of body heat storage.

CONCLUSION

In conclusion, the current study shows that whilst R_{req} is similar to R_{prov} over 105 minutes, alternating bouts of positive and negative body heat storage occur, confirming our first hypothesis. Accordingly, neonates nursed under RWs experienced important fluctuations in both core and skin temperatures beyond the ranges defined by the TNE. This may be caused by a poor correlation between $T_{feedback}$, used to control the flux of heat from the RW and T_{re} . Our results indicate that $T_{feedback}$ does not significantly correlate with changes in T_{re} , which may predispose patients to bouts of passive over/under-heating. Finally, morphological factors did not significantly correlate with R_{req} . Further investigation is required in order to define the optimal method of thermal management when employing the use of RWs in a NICU.

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TABLES

Table 1. Subject Characteristics.

Subject	Age (days)	Gestational Age (weeks)	Weight (grams)	Length (cm)	Body Surface Area (m²)
1	3	34.00	2128	46.5	0.1658
2	4	39.00	2750	47.5	0.1905
3	4	38.57	3727	49.0	0.2252
4	4	37.71	3085	47.0	0.2007
5	6	32.57	1920	44.0	0.1532
6	4	38.14	3288	52.0	0.2180
7	30	29.28	1920	43.0	0.1514
8	30	36.71	2988	51.0	0.2057
9	5	36.28	3100	45.0	0.1968
10	2	36.71	3389	51.0	0.2191
MEAN	9	35.88	2829	47.6	0.1926
SD	11	3.07	636	3.1	0.2710

*Body Surface Area was estimated using Haycock's equation (32).

Table 2. Environmental parameters.

	Ambient Temperature (°C)	Relative Humidity (%)	Barometric Pressure (mmHg)
MEAN	23.4	37	758
SD	0.4	12	3

LEGEND TO FIGURES

Figure 1. A) Heat balance components partitioned into specific heat exchange avenues; rates of evaporation (E), convection (C) and conduction (K) as well as metabolic heat production (M) and heat storage. B) Rate of radiant heat transfer required to attain heat balance (R_{req}) and Rate of radiant heat transfer provided (R_{prov}) by the Radiant Warmer (RW).

Figure 2. Representative example of the pattern in the rate of heat storage (S) over 105 min for one patient nursed under a radiant warmer (RW). Mean S was 0.34 ± 4.32 W.

Figure 3. A matrix plot of rectal temperature (T_{re}) as a function of radiant warmer feedback temperature ($T_{feedback}$); A) Overall, B) during the below set-point condition, C) during the set-point condition, and D) during the above set-point condition. On each plot, the line of identity is denoted by the dashed line and the trendline by the solid black line.

Figure 4. Average net cumulative heat imbalance (kJ) and average positive and negative cumulative heat imbalances (kJ) of 10 neonates nursed under radiant warmers (RW).

Figure 5. Skin Temperature of the Foot, Leg, Abdomen, Chest, Back, Arm, Forehead (in °C) as well as Rectal temperature during below set-point and above set-point conditions of standard NICU care under a Radiant Warmer (RW). Significant differences between conditions are denoted by an asterisk (*) ($p < 0.05$).

Figure 6. Representative of the pattern in the change T_{re} and T_{sk} over 105 min for one patient nursed under a radiant warmer (RW).

Figure 7. Matrix plot depicting the relation between the Rate of radiant heat required for heat balance in each patient (R_{req}) in W and each morphological factor; A) Surface Area-to-Mass ration in kg/m^2 , B) Surface Area in m^2 , C) Length in cm, D) Weight in kg, E) Gestational age in weeks, and F) Post-natal age in days.

FIGURES

Figure 1.

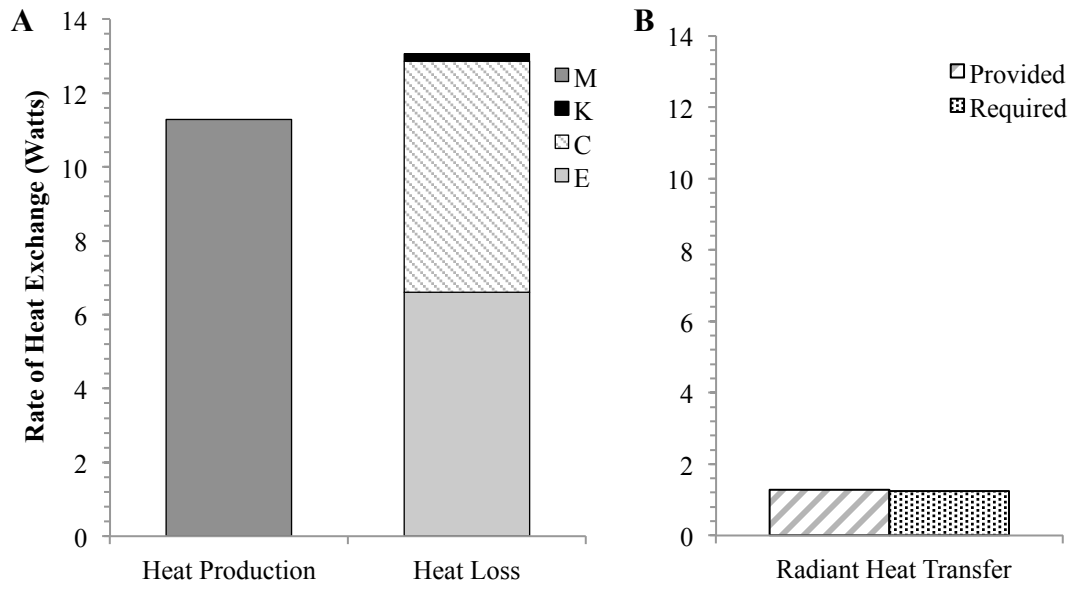


Figure 2.

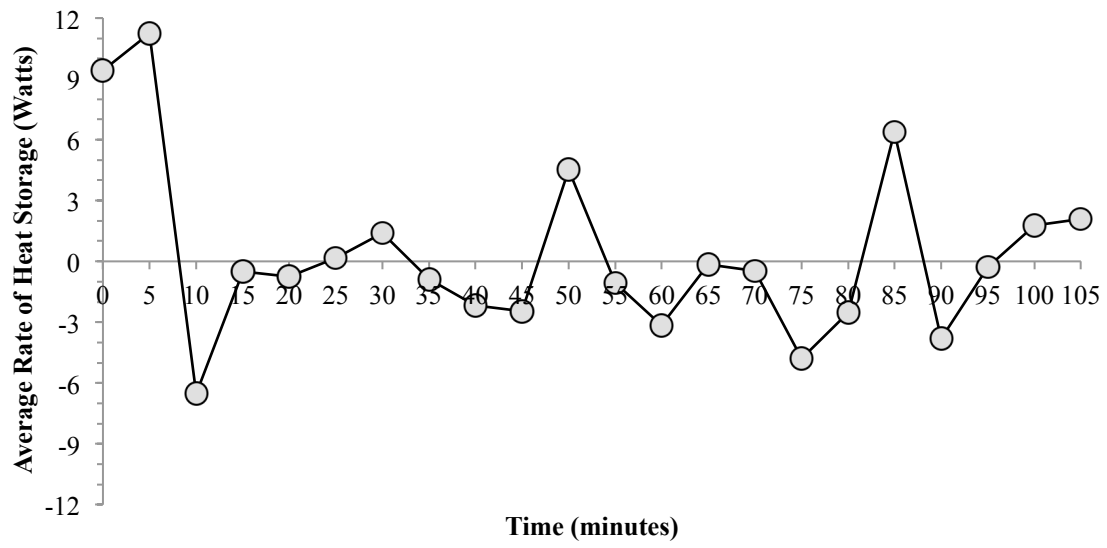


Figure 3.

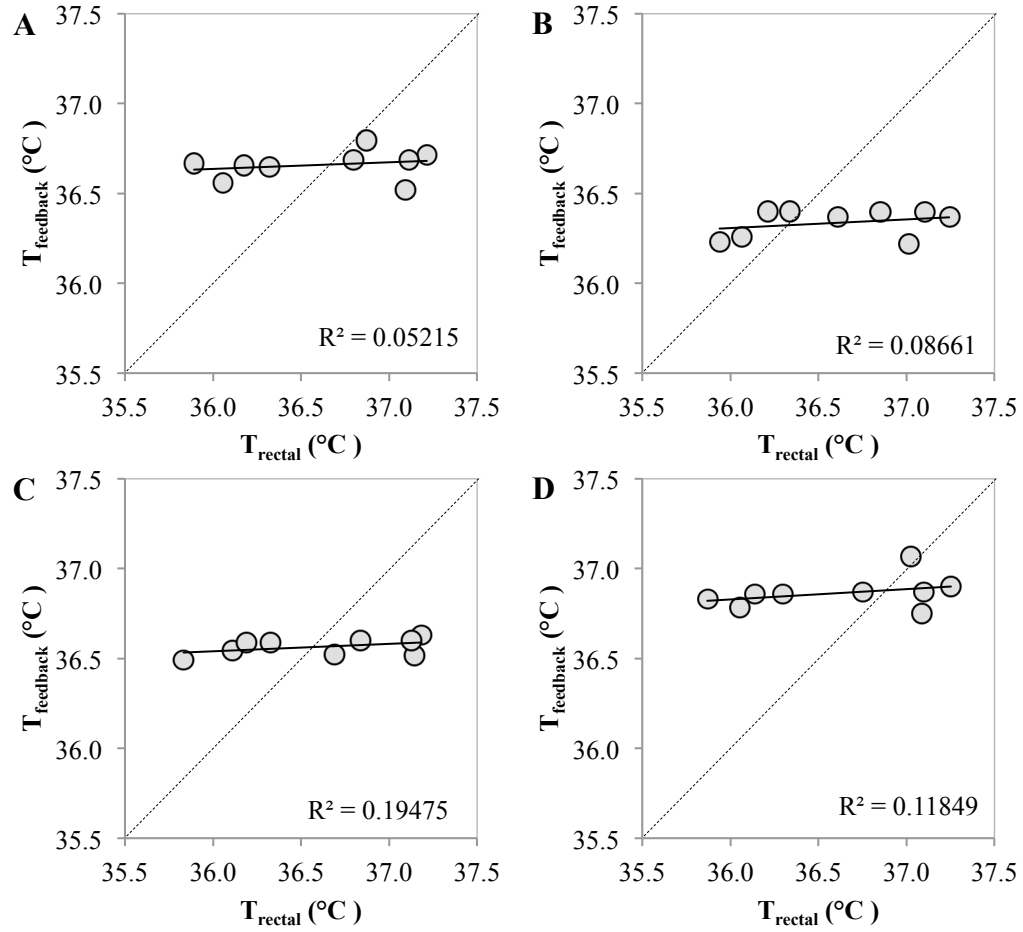


Figure 4.

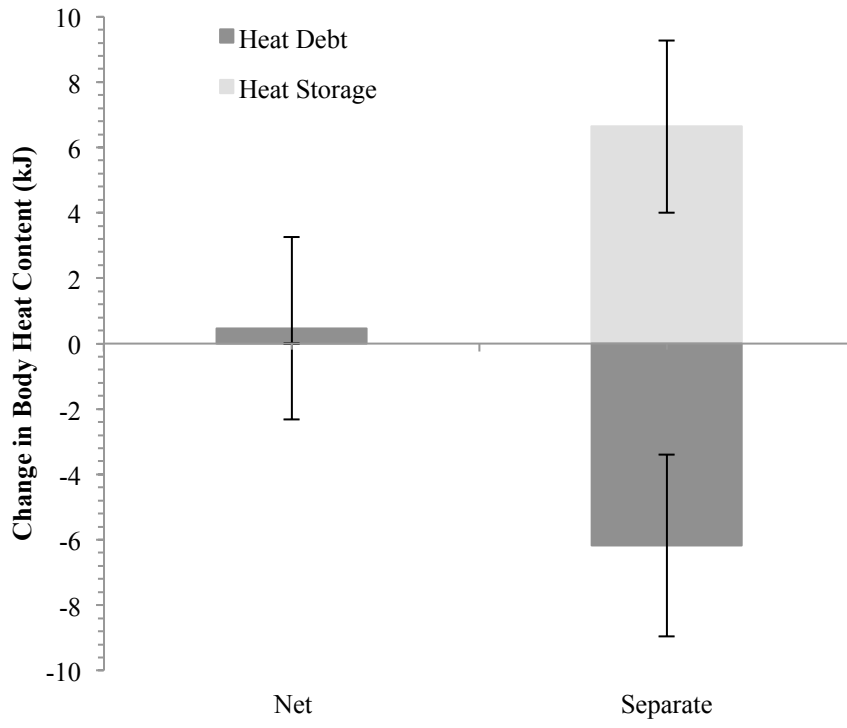


Figure 5.

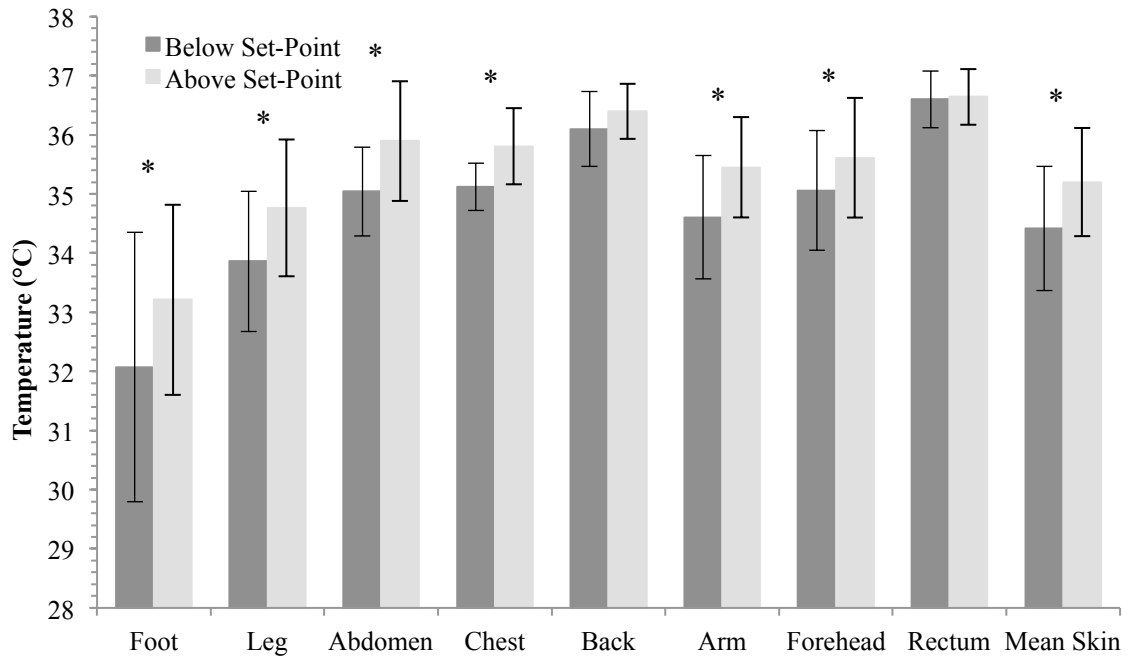


Figure 6.

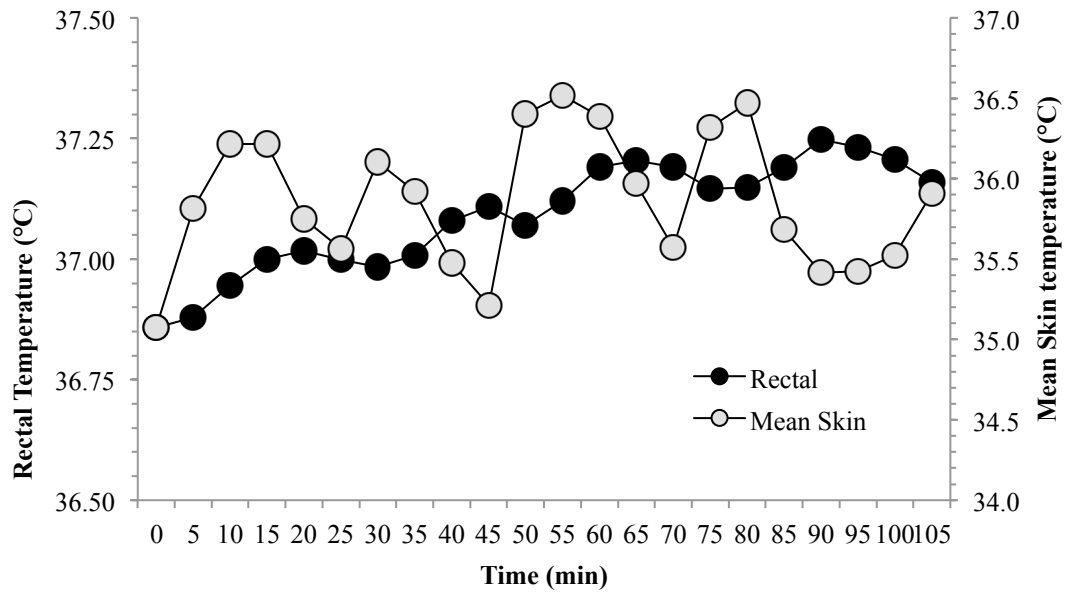
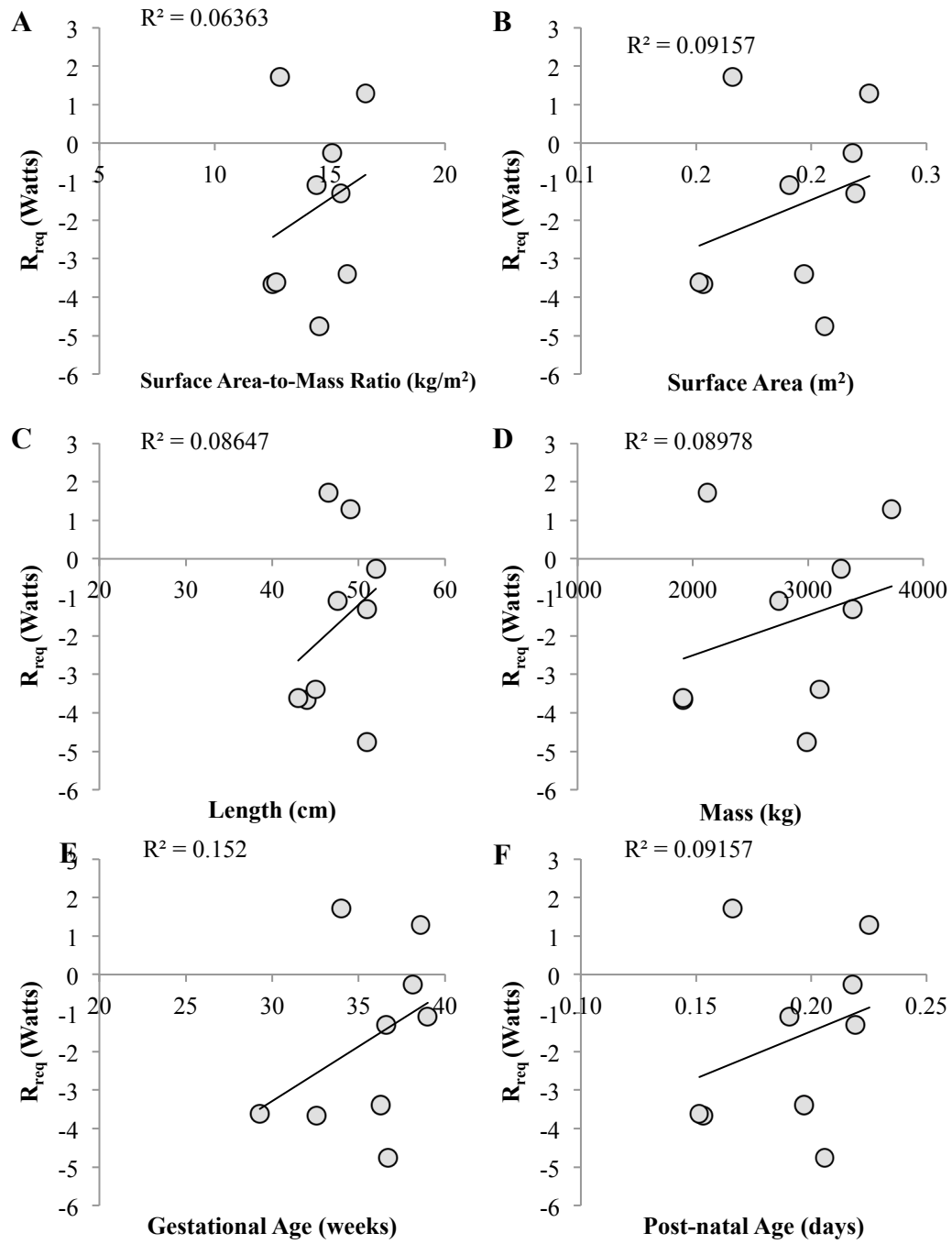


Figure 7.



PART THREE: DISCUSSION ON THE THESIS

For the past 50 years, radiant warmers (RW) have been used in modern NICUs as a method of thermal management for newborns undergoing intensive care. Given the fact that neonates nursed under RWs are exposed to the ambient environment, these devices pose an important challenge with regards to maintaining stable core body temperature. Standard practice stipulates that in order to mitigate metabolic strain whilst maintaining body temperature stable, servo-controlling RW heat output according to axillary skin temperature at 36.5°C is the best thermal management practice to employ when nursing a newborn using a RW (86). To date, several studies have attempted to evaluate the efficacy of the RW at maintaining core temperature and limiting bouts of thermal strain (27, 39, 56, 78). Many of these studies have focused exclusively on the monitoring of thermometric parameters, whilst a few have incorporated a heat balance perspective (27, 39, 91). However, no previous study has rigorously assessed dynamic heat balance in newborns nursed under RWs. Therefore, it was previously unclear whether RWs appropriately maintain heat balance in newborn patients.

The study conducted in the scope of this thesis project aimed to build on previous works and describe the changes in heat balance components during standard care under a RW in stable newborns admitted to a level III NICU. The principal finding of the study is that, while RWs maintain heat balance over a prolonged period of time, the device invokes a sinusoidal pattern of heat imbalance.

Our results demonstrate that the RW invokes a cyclical pattern of large, but brief, deviations away from thermoneutrality by way of passive overheating followed by passive under-heating. This provides unique insight into how the RW regulates the flow of heat provided to the patient. The radiant heat source of the RW responds to changes in

local skin temperature according to a negative feedback signal. In doing so, the RW provides a disproportional amount of radiant heat to the infant when local skin temperature is below the set-point and completely ceases the provision of radiant heat when local skin temperature is above the set-point, effectively maintaining body temperature stable. The primary point of concern is the extent to which whole body thermal status is altered during these periods of heat imbalance. Our data show that in using a negative feedback loop, the RW induces bouts of heat and cold strain. Whilst the study described in the thesis was not designed to evaluate the physiological effects of bouts of thermal stress it is possible that these periods of heat imbalance may increase cardiovascular strain of the patient. Mitigating the magnitude of these bouts of thermal strain is key in appropriate thermal management of a newborn. During the study, 9 out of the 10 patients enrolled did not experience extended episodes of thermal strain, however, one patient experienced a period of acute overheating, characterized peak abdominal skin temperature of 38.1°C, for 30 seconds during which the RW was on high output. The study had to be terminated and the RW had to be turned off in order to allow the patient's skin to cool down despite core temperature not being critically high. Cases such as this underscore the risks associated with the use of RWs. Wheldon et al. (1982) stated that on most commercially available RWs, RW heat output can vary as much as $\pm 25 \text{ W/m}^2$ within periods 2 to 3 min. Paradoxically, the body's requirement for radiant heat does not vary to such an extent, a fact that contradicts the notion of employing a highly variable source of supplemental heat in order to provide a thermoneutral environment.

The changes in heat storage shown in this study highlight the fundamental issue related to the use of RWs to maintain stable body temperature in newborns within an

intensive care setting. Future research should focus on exploring new avenues by which to control the flux of radiant heat emitted by the RW. Rather than supplying radiant heat in direct relation to a measure of local skin temperature, it would be favorable to provide a baseline rate of heat flow that precisely reflects the body's requirement for radiant heat. While this is not a simple concept, by conducting a study on a larger cohort of patients it may be possible to define the predictive criteria that determine a baseline requirement for radiant heat. This information could then be used in order to mathematically derive an algorithm that would be used by the warmer.

In conclusion, this study contributes to the overall knowledge of the control of body temperature in newborns nursed under RWs by highlighting the risks associated with nursing patients using these devices. The data collected during this study provides an essential stepping-stone towards the improvement of thermal management techniques within an NICU.

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