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A mathematical model of premature baby thermoregulation and infant incubator dynamics

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Abstract

A thermodynamic mathematical model of premature infants placed in an infant incubator was developed in order to improve the control algorithm of this incubator. The premature infant's head was represented by a sphere, and the trunk and upper and lower extremities were represented by three cylinders. The sphere and cylinders were divided into two or three concentric layers to represent skin, muscle and core as appropriate for each anatomical structure. Heat flow between adjacent layers was modeled by conduction, and all layers exchanged heat by convection with a central blood compartment. All four skin layers exchanged heat with the environment by convection, radiation, and evaporation. Signals which were proportional to deviations from temperature set points in the brain and in skin were supplied to the model's regulator. The regulator then caused changes in the peripheral blood flow to occur in the skin layers of the appropriate segment in the body. A spatially lumped mathematical model of an infant incubator was developed based on accepted thermodynamic principles. The validity of the baby model was tested in 5 healthy premature newborns (body weight 1,210-1,740 g). The difference between experimental data from direct and indirect calorimetry and the model results averaged 0.1 ± 0.1, 0.2 ± 0.1 and 0.2 ± 0.2 (mean ± SE) °C for the rectum, trunk and head temperatures, respectively. The incubator model showed steady state error less than ± 0.1 °C for air and internal wall temperatures in the air servocontrol mode. The fall in air temperature for the simulation of opening of the front port of the incubator for five minutes was 1.4 °C. After closure of the front panel the incubator model showed a return to the initial temperature in less than 2 minutes. These results are in agreement with published data for this kind of incubator. In conclusion, the model is a good tool for designing improved control algorithms of incubators.

1 Introduction

Premature newborn infants need a closely controlled nursing environment. Preterm newborns are commonly cared for in servo-controlled incubators, with the aim of providing an optimal nursing environment, while allowing close observation of and access to the infant for therapeutic intervention [1,2]. In steady-state, modern incubators maintain accurate control of the infant's environment. When the environment is challenged, as when changing a diaper, modern incubators cannot maintain a stable, and accurate thermal environment [3,4].

As part of a proposed redesign of the incubator controller, we have developed a thermodynamic mathematical model describing the complex interaction between a premature infant and an incubator. The thermodynamic model requires the infant's gestational age, postnatal age, and weight, and room temperature and incubator humidity. The output is a minute-by-minute prediction of the subject's temperatures (different skin and core site temperatures) and of the incubator's temperatures (air, wall and mattress temperatures). We validated the model by comparing the model's predicted response to measured data in five infants, and with published.

2 Modelling Design

2.1 Premature Baby Compartmental Model--Overview

The model follows the general scheme proposed by Stolwijk [5]. The model divides the body into 4 segments (head, trunk, upper limbs and lower limbs) and 11 compartments (3 layers for the head and trunk segments, 2 layers for each "limbs" segment plus the connecting blood compartment). Each body compartment is characterized by a temperature, volume, surface area, density, specific heat, thermal conductivity, and metabolic rate. A list of symbols for this characterization is presented in Table 1. Values of the physical properties for the different tissues were obtained from the literature [6,7,8] and are summarized in Table 2.

Because premature infants typically do not sweat and do not shiver, these self-regulatory mechanisms were not included. Work or exercise was not included because premature babies do not substantially increase their metabolism with movement [2,6]. Thus, the model tries to simulate the premature baby's response in a near thermoneutral regulated environment where just the vasomotor system is the active controller in the thermoregulation.

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Table 1. List of Symbols and Characterization.

	SKIN	CORE	MEDIUM	FAT	UNITS
TEMPERATURE	TS_i	TC_i	TM	TF	^oC
VOLUME	SV_i	CV_i	MV	FV	m^3
SURFACE AREA	SA_i	--	--	--	m^2
DENSITY	ρ_S	ρ_{Ci}	ρ_M	ρ_F	$kg \cdot m^{-3}$
SPECIFIC HEAT	Cp_S	Cp_{Ci}	Cp_M	Cp_F	$J \cdot kg^{-1} \cdot {}^oC^{-1}$
CONDUCTIVITY	k_S	k_{Ci}	k_M	k_F	$W \cdot m^{-1} \cdot {}^oC^{-1}$
METABOLIC RATE	--	MET_i	MM	MF	W

i=1:head, 2:trunk, 3:upper limb,4:lower limb.

Table 2. Physical Properties of Tissues and Blood

COMPARTMENT	DENSITY	SPECIFIC HEAT	CONDUCTIVITY
SKIN	1000	3766	0.209
HEAD CORE	1050	3694	0.527
TRUNK CORE	1030	3539	0.430
LIMBS CORE	1030	3020	0.404
MEDIUM LAYER	1030	2270	0.471
FAT LAYER	1050	2510	0.160
BLOOD	1000	3770	--

Density ($kg \cdot m^{-3}$), Specific heat ($J \cdot kg^{-1} \cdot {}^oC^{-1}$), and Conductivity ($W \cdot m^{-1} \cdot {}^oC^{-1}$)

2.1.1 Heat Balance Equations

The energy balance equations were derived for each compartment separately. The core heat balance equation is equal for the four different body segments (i=1,2,3,4):

$$CC_i \frac{\partial TC_i}{\partial t} = MET_i + CDTC_i + CVC_i + RES_i \qquad (1)$$

where $CC_i = CV_i \, \rho_{Ci} Cp_{Ci}$ is the heat capacity of the core layer of the segment i, in $J \cdot {}^{o}C^{-1}$ (See Table 1 for a description of CV_i, ρ_{Ci}, and Cp_{Ci}). The metabolic rate MET_i for the core was assumed to be a percentage of the total metabolic rate. Division of the metabolic rate between the compartments was based partly on the literature and partly on the original model [6,9,10]. Percentage breakdown of total heat production among compartments is shown in Table 3. $CDTC_i$ is the heat transferred between the core and the previous tissue layer by conduction; CVC_i is the heat transferred to the core by convection with the blood, and $RES_i = REW_i\ Q_{res}$ (W) is the heat loss to the environment by respiration. The heat loss by respiration RES_i was assumed to be zero for the limbs and a percentage of the total heat loss by respiration for the head and trunk.

Table 3. Percentage of Total Heat Production for the Different Core Compartments.

COMPARTMENT	PERCENTAGE
HEAD	68.85%
TRUNK	22.93%
UPPER LIMB	2.00%
LOWER LIMB	4.00%

The heat balance equation for the medium and fat layers were written as follows:

$$CM \frac{\partial TM}{\partial t} = MM + CDM + CVM \tag{2}$$

$$CF \frac{\partial TF}{\partial t} = MF + CDF + CVF \tag{3}$$

where $CM = MV\ \rho_M\ Cp_M$ and $CF = FV\ \ \rho_F\ Cp_F$, and are the heat capacity of the medium and fat layers, respectively, in $J \cdot {}^{o}C^{-1}$. The metabolic rates MM and MF for the medium and fat layers were assumed to be 1.15 and 1.07 per cent of the total metabolic rate, based on the Stolwijk's original model [5]. CDM and CDF are the heat transferred by conduction between the described layers, and the core and skin layers; CVM and CVF are the heat transferred to the medium and fat layers by convection with the blood, respectively.

The skin heat balance equation is the same for the four different body segments ($i=1,2,3,4$):

$$CS_i \frac{\partial TS_i}{\partial t} = CDT_i + CVb_i + CVT_i + RAD_i + EVP_i \qquad (4)$$

where $CS_i = SV_i\, \rho_S\, Cp_S$ is the heat capacity of the skin layer of the segment i, in $J \cdot {}^oC^{-1}$. CDT_i is the heat transferred between skin and the adjacent tissue layer by conduction; $CVbi$ is the heat transferred to the skin by convection with the blood; CVT_i and RAD_i (in Watts) are the heat losses to the environment by air convection and radiation, respectively. The rate of heat exchange, CVT_i, is related to the temperature difference between the local skin Ts_i (°C) and the air Ta (°C), and to the exchanging surface area of the body segment, SA_i (m^2). CVT_i also depends on the convection coefficient, h_c ($W \cdot m^{-2} \cdot {}^oC^{-1}$) [11], and is found from:

$$CVT_i = h_c\,(Ts_i - Ta)\,SA_i \qquad (5)$$

The convection coefficient h_c is strongly dependent on air velocities, and has been experimentally determined by several investigators [11,12]. Heat lost or gained by the skin due to radiation can be described by the Stefan-Boltzmann's law [12]:

$$RAD_i = \sigma\, SA_i\, e_S\, [(Ts_i + 273)^4 - (Tw + 273)^4] \qquad (6)$$

where e_s is the radiant emissivity of the skin, σ is the Stefan-Boltzmann constant (5.67×10^{-8} $W \cdot m^{-2} \cdot K^{-4}$), Ts_i and T_W are the local skin's and the surrounding temperatures in °C, and SA_i (m^2) is the local skin area. EVP_i (W) is the heat loss to the environment by evaporation. It was assumed that heat loss by evaporation EVP_i is due to local transcutaneous water loss (or diffusion) TWL_i($g \cdot h^{-1} \cdot m^{-2}$):

$$EVP_i = \frac{0.58\ TWL_i\ SA_i}{0.86} \qquad (7)$$

where SA_i is the segment skin area and the constants are for unit conversion. The local transcutaneous water loss was calculated by applying the Ultman equation [13]:

$$TWL_i = k\,(P_{Si} - \frac{RH\,Pa}{100}) \qquad (8)$$

where RH (%) is the ambient relative humidity; Pa and P_{Si} (kPa) are the equilibrium water vapor pressure at Ta and TS_i, respectively; k ($g \cdot h^{-1} \cdot m^{-2} \cdot kPa^{-1}$) is a mass transfer coefficient which depends on the gestational GA (weeks) and postnatal age PNA (days).

2.2 Incubator Compartmental Model--Overview

The model describes a single wall, rectangular incubator with forced convection heating, similar to that described by Simon et al. [14]. This model was partitioned into three distinct homogeneous compartments: the incubator wall, the incubator air space, and the mattress. The environment, or room, was considered an infinite sink for the energy leaving the incubator system, therefore the incubator dynamics did not affect the room temperature.

2.2.1 The Incubator Wall

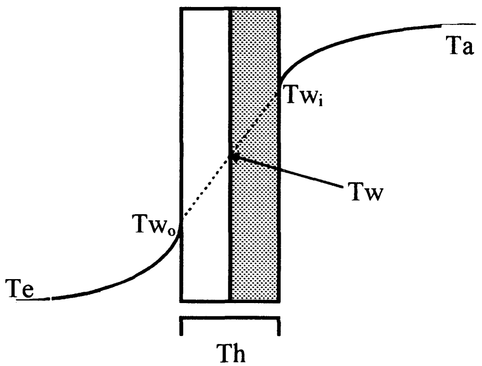

Figure 1. Incubator Wall Model. *Te* , *Two*, *Tw*, *Twi* and *Ta* (°C) are the room, external surface, wall compartment, internal surface and air space temperatures, respectively. *Th* (m) is the wall thickness.

The model for the incubator wall was composed of three parts: the external surface, the wall compartment, and the internal surface. The model simulating wall was derived from the energy balance on the control volume strip *Th/2* wide (Fig. 1). The heat balance equation for the wall's external surface was written as follows:

$$Cw\frac{dTwo}{dt} = Qcdout - Qcvout - Qri \tag{9}$$

where *Two* (°C) is the temperature of the outer surface, and *Cw* ($J \cdot {}^{o}C^{-1}$) is the thermal capacitance of the control volume strip. This equation assumes that the wall's external surface loses heat to the room environment by convection *Qcvout* (W) and radiation *Qri* (W), and gains heat by conduction *Qcdout* (W) from the mid-surface of the wall (wall compartment). The equations describing convective and radiative heat loss from the incubator's external surface are similar to Eq. (6) and Eq. (7), respectively. The heat conducted from the wall compartment to the external surface was described by the following equation [15]:

$$Qcdout = \frac{Kw\,Aw}{Th/2}(Tw - Two) \tag{10}$$

where *Kw* ($W \cdot m^{-1} \cdot {}^{o}C^{-1}$) is wall conductivity, *Aw* (m^2) is the wall surface area, *Th* (m) is the wall thickness, and *Tw* and *Two* (°C) are the wall compartment and the external surface temperatures, respectively.

The heat balance equation for the wall compartment was written as follows:

$$(2\,Cw)\frac{dTw}{dt} = Qcdin - Qcdout \tag{11}$$

This equation assumes that the wall compartment loses heat to the external surface, *Qcdout* (W), and gains heat from the internal surface, *Qcdin* (W), both by conduction. The equation describing the heat conducted from the internal surface to the wall compartment is similar to Eq. (10). Finally, the internal surface was modeled in the same way as the external surface.

$$Cw\frac{dTwi}{dt} = Qcvin + Qr - Qcdin \tag{12}$$

This equation assumes that the wall's internal surface loses heat to the wall compartment by conduction *Qcdin* (W), and gains heat by convection *Qcvin* (W) from the air space of the incubator, and by radiation *Qr* (W) from the premature baby. The equations describing convective and radiative heat gained by the incubator's internal surface are similar to Eq. (6) and Eq. (7), respectively.

2.2.2 The Incubator Air Space

The lumped air space compartment loses heat through convection with the incubator walls (*Qcvin*) and the mattress (*Qmat*), but gains heat from the incubator heater (*Qheat*). It also can lose or gain heat from the baby (*Qe* and *Qcva*). The heat balance equation for this compartment was written as follows:

$$Ca\frac{dTa}{dt} = -Qcvin - Qmat + Qheat + Qb + Qcva \tag{13}$$

where *Ca* ($J \cdot {}^{o}C^{-1}$) is the air space thermal capacitance. The equations describing the convective heat loss by the incubator's air space to the wall and to the mattress were similar to Eq. (6). The equations for the heat gained from the baby due to evaporation *Qe* and air convection *Qcva* were described by the sum of the respective baby model equations. The heat exchange with the heater was described by the following infiltration equation [15]:

$$Qheat = V_a \rho_a Cp_a (Ta - Tha) \tag{14}$$

where V_a ($m^3 \cdot s^{-1}$) is the flow rate of air into the incubator, ρ_a ($kg \cdot m^{-3}$) is the density of the air, Cp_a ($J \cdot kg^{-1} \cdot {}^oC^{-1}$) is the blood specific heat, Ta (°C) is the air space temperature, and Tha (°C) is the temperature of the heated air entering the air space.

2.2.3 The Mattress

The lumped mattress compartment was assumed to gain heat by convection from the air space (*Qmat*) and by conduction from the baby (*Qcm*), while the heat conduction between the mattress and the walls was considered negligible, therefore:

$$Cm \frac{dTm}{dt} = Qmat + Qcm \tag{15}$$

where Cm ($J \cdot {}^oC^{-1}$) is the mattress thermal capacitance.

3 Model Validation

3.1 Baby Model Validation

The compartmental baby model was validated using data taken from five premature infants whose heat production was measured in an infant calorimeter [16]. The five subjects had weights from 1,210-1,740 g (median 1,630 g) and gestational age from 27-32 wk (median 29 wk). These data were collected as follows: Subsequent to a feeding, the infant was placed in a gradient-layer calorimeter developed at the University of Iowa [16]. After an equilibrating period of thirty minutes, data collection was initiated. Trunk, head, leg and feet skin temperatures were sampled every five minutes for eighty-five minutes. The rectal temperature was recorded every minute for eighty-five minutes. All of the remaining data were taken every minute for eighty-five minutes. The remaining data include oxygen consumed, carbon dioxide produced, humidity ratio in and out, heat of vaporization in and out, direct calorimetry and indirect calorimetry. Humidity, the air temperature and the wall temperature inside the calorimeter, the infant's weight, gestational age, and postnatal age were.

For the different baby files a simulation was done maintaining the calorimeter environmental conditions (same air temperature, wall temperature, humidity, etc.). The average of the skin temperatures and rectal temperatures were used as skin and core setpoints respectively. Finally, the indirect metabolic heat production was used as input to the compartmental baby model simulation.

The mean absolute error was calculated between the time courses of the observed and predicted temperature responses. This gave a quantitative measure for the average difference between observed and predicted time courses in degrees Celsius, and enabled direct comparison with the published results from Stolwijk's model validation by Konz et al. [17].

We tested differences between our model and the observed responses with an ANOVA at $P < 0.05$.

3.2 Incubator Model Validation

The incubator model was validated by comparing computer simulation with data from published experiments involving forced-air convective incubators. Sjörs et al. [1] examined the performance characteristics of seven available incubators. From those incubators, we used our incubator model to simulate an Airshields Isolette C100 incubator in the proportional air servo-control mode. The incubator model was used to simulate an empty incubator using proportional air servocontrol. The initial conditions were given for a room at 22.5 °C, and wall and mattress temperatures at 24 °C. The incubator set point was set at 34 °C. This simulation was used to validate whether our model was capable of representing the above incubator responses to a five-minute front port opening in both steady-state and transient conditions.

The five minutes opening of the incubator ports was simulated by a perturbation that modified the air space equation (Eq. 13). This perturbation was represented as follows:

$$\frac{dTa'}{dt} = Ko\,(Te - Ta) \qquad (16)$$

where dTa'/dt represents the perturbation, Ta is the air temperature, Te the environmental temperature, and Ko the proportional constant that represents the infiltration rate across incubator ports.

The mean absolute error was calculated between the time courses of the published and predicted temperature responses. This gave a quantitative measure for the average difference between published and predicted time courses in degrees Celsius. Further validation was done with a **t**-test of the temperature time courses of the model response against the published temperature values [1].

3.3 Baby-Incubator Steady-State Validation

Bell and Rios [18] measured heat production and loss by partitional calorimetry on eight premature newborn infants. They also measured mean skin and rectal temperatures from the babies, as well as air and wall temperatures from the incubators. The incubator with the baby model was used to simulate the system using proportional skin servocontrol to mimic the published experimental conditions. All of the results were compared between the experimental data and the model predictions using the **t**-test for paired observations. We considered differences significant at $P < 0.05$.

4 Results

4.1 Baby Model Validation

The calculated mean absolute error between the time courses of the observed and predicted temperature responses varied between 0.1 and 0.6 °C (Table 4). Comparing these results with those obtained for the Stolwijk's model they seem to be reasonable (Table 5). Figure 2 shows the model predicted and measured core of the trunk temperature for a typical data set (GA=32 wk) during 85 minutes.

Table 4. Mean absolute error between the measured data and simulated temperatures over a 85 minutes period for the different babies. (°C)

Baby #	Skin of the Head	Skin of the Trunk	Rectal
1	0.07	0.05	0.05
2	0.59	0.38	0.14
3	0.07	0.18	0.14
4	0.21	0.22	0.13
5	0.09	0.39	0.09

Table 5. Mean absolute error between the real data and simulated temperatures over a 85 minutes period, for the different body places

Place	Stolwijk Model	Baby Model (SD)
Head	0.4 °C	0.2 °C (0.2)
Trunk	0.6 °C	0.2 °C (0.1)
Rectal	0.1 °C	0.1 °C (0.04)

Finally, the ANOVA test showed no statistical difference between the time courses of the observed and predicted temperatures for all the measured sites ($P > 0.05$).

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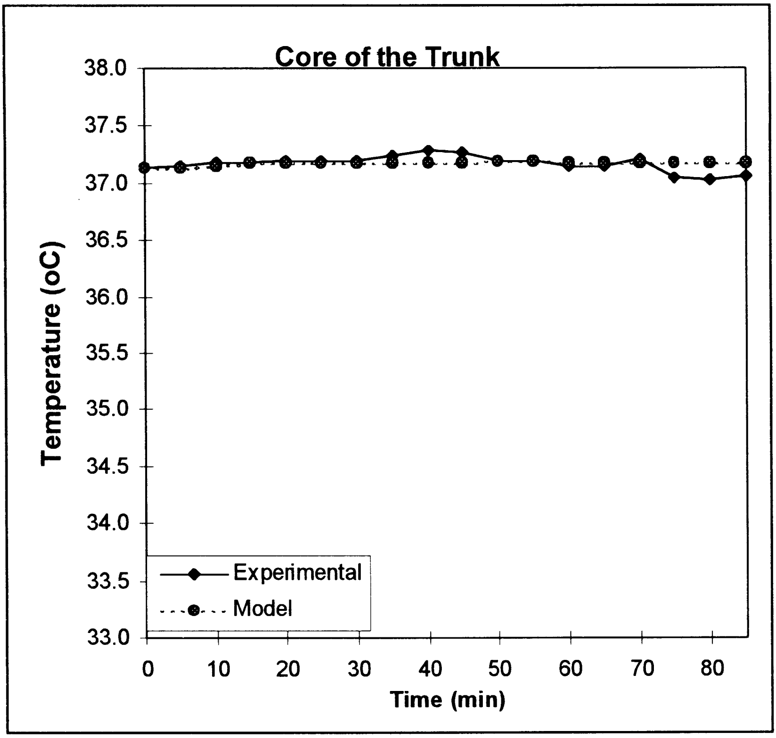

Figure 2. Trunk Core Temperature for a premature infant with GA of 32 weeks.

4.2 Incubator Model Validation

Table 6. Steady-State Temperatures for the Empty Incubator.

	MODEL	REAL [1]
Ta	33.9 °C	34.0 °C
Twi	31.3 °C	31.4 °C
Two	30.4 °C	------
Tm	33.9 °C	34.0 °C

The steady-state response of the model showed values for air, wall and mattress temperatures similar to the published values for the Airshields Isolette C100 incubator [1,18]. Results are summarized in Table 6. When the five minute opening of the incubator ports was simulated, time recovery for the air temperature was 2 minutes which agrees with the results for the Isolette C100 incubator published by Sjörs et al.[1] (Fig. 3). The calculated mean absolute error between the time courses of the observed and predicted temperature responses was 0.12 ± 0.09 °C (SD). Finally, the paired t-test show no statistical difference between the time courses of the observed and predicted temperature responses (P >0.05).

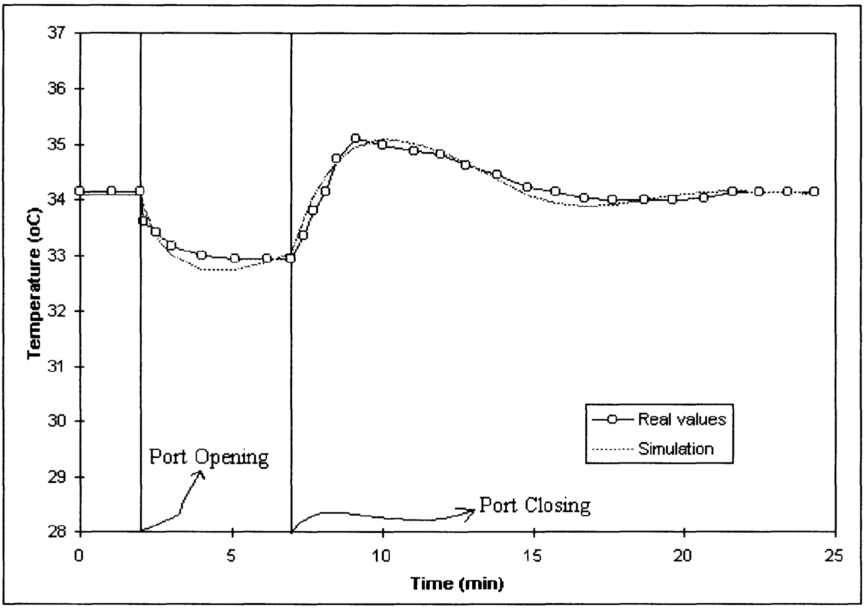

Figure 3. Changes in air temperature (°C) when the front panel is opened 5 minutes.

4.3 Baby-Incubator Steady State Validation

The results of combining the baby and incubator model showed good agreement with the experimental results reported by Bell et all. [18]. There was no difference between the model-predicted temperatures and heat loss rates and those directly measured from the infants. The largest error, thought no statistically significant, was in the evaporative heat loss which was underestimated by the model. Results are summarized in Table 7.

Table 7. Heat exchange data for premature infants and the model in a single-walled incubator[1]

		Temperatures (oC)						Heat production and loss (kcal/kg/h)			
Subject	CASE	Tabd	Ts	Trect	Tair	Twall	Top	HL	E	R	C
1	REAL	36.5	36.4	37.3	34.4	30.3	31.9	2.74	0.82	1.37	0.55
	MODEL	36.5	36.4	37.3	33.9	30.5	31.9	2.74	0.62	1.33	0.79
2	REAL	36.5	36.5	37.1	36.4	32.7	34.2	2.08	0.92	0.94	0.22
	MODEL	36.4	36.2	37.3	35.4	31.5	33.1	2.08	0.70	1.16	0.21
3	REAL	36.4	36.4	37.1	35.5	31.5	33.5	2.39	0.53	1.21	0.65
	MODEL	36.5	36.3	37.3	34.7	31.1	32.6	2.39	0.62	1.29	0.48
4	REAL	36.5	36.3	37.3	35.5	32.7	33.8	1.85	0.61	0.90	0.34
	MODEL	36.5	36.3	37.2	36.2	32.7	34.1	1.85	0.90	0.92	0.03
5	REAL	36.4	36.1	37.3	34.3	31.8	32.8	2.28	0.61	1.04	0.63
	MODEL	36.6	36.5	37.3	35.3	32.5	33.6	2.28	0.86	0.98	0.44
6	REAL	36.4	36.5	37.0	37.4	32.7	34.6	1.94	1.24	0.97	-0.27
	MODEL	36.4	36.2	37.1	36.1	31.8	33.5	1.94	0.78	1.12	0.04
7	REAL	36.3	36.3	37.1	34.5	31.6	32.8	2.65	0.88	1.12	0.65
	MODEL	36.6	36.5	37.3	34.2	31.4	32.6	2.65	0.73	1.21	0.71
Mean	REAL	36.4	36.4	37.2	35.4	31.9	33.4	2.28	0.80	1.08	0.40
	MODEL	36.5	36.4	37.3	35.1	31.7	33.0	2.28	0.74	1.14	0.39
P value		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

[1] Abbreviations: Tabd, abdominal skin temperature; Ts, mean skin temperature; Trect, rectal temperature; Tair, incubator air temperature; Twall, mean incubator wall temperature; Top, operative temperature; HL, total heat loss; E, evaporative heat loss; R, radiative heat loss; C, convective heat loss. [2] Two-tailed t-test for paired observations. NS indicates $P > 0.05$.

5 Discussion

We have presented and validated a thermodynamic model of a premature infant, a thermodynamic model of an incubator, and a model of the complex thermodynamic interaction between an infant and an incubator. We have showed that model-predicted temperatures and heat fluxes agree with data extracted from the literature, and data obtained from experiments conducted on premature infants.

We modified the model first proposed by Stolwijk [5] in order to simulate the thermodynamic conditions of a human newborn infant. There are a number of differences between the adult and newborn thermoregulatory systems that we have modeled. The percentage of the total body metabolic heat production in the brain of adults is approximately 20% [5], while the percentage of the total body metabolic heat production in the brain of a newborn baby is approximately 70% [9]. The thermal conductance of a 4-kg newborn baby is approximately three times that of the adult, and for a smaller 1-kg premature baby, the conductance is approximately five times that of the adult [19]. The model's autonomic controller was also adjusted to account for the differences in regulation in the premature infant. These differences include metabolism of brown fat, and an underdeveloped sweating and shivering response to hot and cold environments. We also simplified Stolwijk's model, which has twenty-five compartments, by including only eleven compartments.

The incubator model proposed by Simon [14] represented the wall of the incubator as one thermodynamic compartment. We found that it is difficult to accurately model the heat flux across the wall of the incubator with a single compartment. Therefore in our model the incubator wall was represent by three compartments, one describing the inner surface, one describing a virtual middle surface, and one describing the outer surface. This change allows accurate simulation of the heat flux across the wall due to a temperature gradient between the environment (room temperature) and the interior of the incubator (inside air temperature).

The baby model and the incubator model have been separately validated with dynamic tests. Thus the baby model was able to accurately predict body temperatures of infants as time progressed. The incubator model was able to accurately predict the inside air temperature when the incubator lid was opened to room air for a period of five minutes. The results that we present for the combined baby-incubator model were only tested with static conditions. The dynamic validation for the combined baby-incubator model is presently being done.

In conclusion, we have presented a model that is a useful tool for studying the thermodynamic behavior of premature infants, and for modernizing the design of human incubators.

Key Words:

Thermodynamic Model.
Premature Infant.
Infant Incubator.

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