The Mathematical Modelling of Cooling and Rewarming Patients during Cardiac Surgery

Marcus Tindall[*] *Mark Peletier*[†] *Joyce Aitchison*[*]
Simon van Mourik[‡] *Natascha Severens*[†]

Abstract

The process of cooling bodies, by the use of a heart lung machine (HLM), is utilised in a number of surgical procedures primarily to reduce the metabolic rate of the organs and hence their consumption of oxygen. On completion of surgery the blood is rewarmed by the HLM. A major consequence at the end of this process is afterdrop: a rapid decrease in the core organ temperature as a result of spatial temperature differences between the core organs and remainder of the body, which can lead to post-operative complications. This report details two mathematical models developed to understand heat transfer processes between the core organs, rectal region and peripheral body parts (primarily skin, muscle and fat). A one compartment spatially independent model, describing the temperature distribution of a single tissue type through which blood perfuses, shows that temperature dependent perfusion reproduces the observed differences in blood and tissue temperatures, whilst temperature independent perfusion does not. The model is extended to account for heat transfer between the blood pool (core), rectal regions and periphery. This three compartmental model is able to qualitatively reproduce the observed temperature differences in the three regions. Analysis of the model shows that a period of constant warming at the end of the rewarming period has a positive effect in reducing afterdrop.

1 Introduction

The cooling of the body of patients during surgical procedures has been used for a number of years in a variety of operations [1]. Cooling is primarily used to reduce the metabolic rate of organs within the body and thus the amount of oxygen they consume. This has two purposes: (1) it is less likely that irreparable damage to vital organs will occur due to oxygen deficiency; and (2) it allows the surgeon more time should some unusual complications occur during the surgical procedure.

In this report we are concerned with the application of the procedure to patients undergoing cardiac surgery. During cardiac surgery with cardiopulmonary bypass - the majority of cardiac surgical interventions - cooling is performed by means of a heart lung machine (HLM). The process consists of six distinct phases as detailed below and shown in Figure 1.

[*] University of Oxford
[†] Technische Universiteit Eindhoven
[‡] Universiteit Twente

1. The patient is anaesthetised whereby the body temperature drops naturally by approximately 2°C (not shown in Figure 1).

2. The first stage of the surgery begins. This consists of the chest cavity being opened and the area around the heart (muscle and tissue) being prepared for the main surgical procedure.

3. The body is connected to a HLM whereby the blood is circulated through the machine and the temperature of the blood lowered at the instruction of the cardiac surgeon in agreement with the perfusionist. Blood from the HLM generally enters the body through a tube inserted in the aorta. A HLM contains a simple heat-exchanger whereby the cooling or warming fluid is generally water.

4. The main cardiac surgical procedure takes place, during which the body is kept at a constant cooled temperature. The temperature during surgery depends on the surgical intervention e.g. for aorta valve replacements and coronary artery bypass grafts 30°C is a common temperature, whilst during surgery on the aortic arch the patient is cooled to 16-18 °C.

5. Following completion of the surgical procedure the blood is warmed at a steady rate. Rewarming must not take place too quickly for large spatial or temporal differences in temperature can cause damage to cells and, on the larger scale, irreversible damage to organs.

6. Once the core organs have reached a certain temperature the patient is disconnected from the HLM and the temperature of the body allowed to self-equilibrate. This often results in a phenomena known as afterdrop: an observed decrease in the temperature around the core organs. The afterdrop effect is considered to be a result of the large temperature difference between the core and peripheral regions. Patients who experience a large afterdrop in temperature often take longer to recover and may experience further post-operative complications. Thus clinicians try to minimise the afterdrop effect as much as possible.

The current protocol for both cooling and rewarming patients is very much an *ad hoc* procedure, i.e. it relies on the expertise and experience of the surgeon, perfusionist, and anaesthetist. For instance, in the course of recent years the target temperature for average operations, such as aortic valve replacements and coronary artery bypass grafts, has risen from 28°C to 30°C, as the result of clinical experience.

Previous mathematical modelling in the area has focused on developing models describing the cooling/rewarming process in specific body parts as well as the temperature distribution throughout the whole body, the models varying in both detail and complexity. Pennes [4] described the temperature distribution in the tissue and arterial blood of the human forearm using a standard formulation of the heat equation which takes account of perfusion and possible heat sources and/or sinks. Curtis and Trezek [1] have formulated a five compartmental model which accounts for heat transfer between the core organs, muscle, fat, skin and the blood.

Fiala et al. [2, 3] have developed a computational model for predicting human thermal body regulation. They consider the body to consist of two parts: the passive system and the active system. The passive system describes heat transfer both

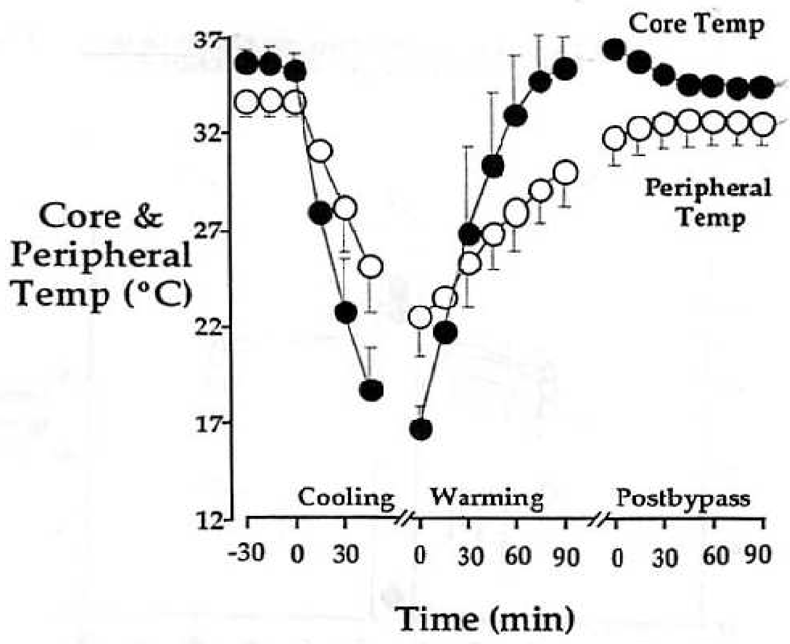


Figure 1: A typical temperature curve for the cooling and rewarming process. Taken from [5].

within the body and between the body and the external environment. The active system describes the thermoregulatory responses of the body when the body temperature deviates from its normal temperature e.g. vasodilation, vasoconstriction, shivering or sweating. They construct a whole-body model of an average human (73.5kg, 14% body fat) which consists of 15 spherical or cylindrical segments representing the head, arms, thorax, etc. Pennes' equation [4] is applied to each of the segments with the appropriate boundary and initial conditions.

The Study Group was asked to focus on developing suitable mathematical models which would:

1. help explain the observed differences in temperatures recorded in different parts of the body (mainly the core organs, rectum and peripheral body regions - skin, fat and muscle);

2. assist in developing more robust and physiologically based cooling and warming protocols for different size patients, e.g. fat versus thin, tall versus short; and

3. provide insight into possible causes or reasons for the afterdrop effect occurring and how this effect may be reduced or remedied.

This report details two models developed during the Study Group to help answer these questions. Section 2 details experimental data available on the problem. Sections 3 and 4 detail two models: the first is a simple model developed in order to

Body part	Perfusion rate - W [l/(s · m^3)]	Tissue conductivity - D $\times 10^{-7}$ [m^2/s]
Main Organs	4-10	1.0-2.0
Muscle	0.5	1.6-4.0
Skin	1-10	2.0
Fat	3.6×10^{-3}	0.64

Table 1: Typical perfusion and conductivity coefficients for tissue in different parts of the human body. Taken from [2].

reproduce some of the observations obtained in the cooling and rewarming procedure. The second model or 'Amsterdam' model extends the first, but focuses on developing a model specifically targeted at explaining the observed temperature differences between the core organs (including the brain), rectum and peripheral regions. Comparisons between the models are made and their application and areas of possible further development are discussed in Section 5.

2 Clinical and experimental data

A number of data sources exist on the temperature of bodies during both the cooling and rewarming process for different surgical procedures. Given the detail of the model developed by Fiala et al. [2, 3] their papers provide a good source of data on rates of heat transfer (via both perfusion and conduction) and the capacitance of specific body parts and organs as shown in Table 1. Here perfusion refers to the amount of fluid (blood) moving through a certain volume of tissue per unit time. By means of this blood flow, convective heat transfer takes place. This is in contrast to conductive heat transfer, which refers to the transport of heat through tissue or the surrounding medium (air) which is dependent upon the conductivity of the medium.

The large variation in perfusion rates for different parts of the body detailed in Table 1 causes us to think carefully about how this affects heat transfer through the body in the context of the surgical cooling/rewarming procedure. As blood from the HLM enters the aorta it is pumped around the body, reaching the core organs first. Thus given the high rate of perfusion in this area the temperature quickly rises to that of the blood temperature. However, in regions which are not so well perfused such as the peripheral regions, in particular fat, the rate of heat transfer will be greatly reduced. Indeed heating such regions will take considerably longer although the tissue conductivity of heat between the core and periphery is approximately the same.

Given this data, in what follows the body is broadly considered to consist of three lumped regions:

1. the core organs - the main organs of the body found between the lower abdomen and up to and including the brain;
2. the rectum - including the large and small intestines and the rectal area; and
3. the periphery - muscle, skin and fatty tissue.

As the thermoregulatory responses of the body (the active system) are impaired during cardiac surgery, we will only consider passive heat processes.

3 A one-compartment model

We begin by formulating a simple one-compartment model which accounts for the transfer of temperature between the blood and tissue. In this model and the one detailed in Section 4 we assume that the temperature distribution is spatially homogenous and we are only interested in time dependent heat transfer between the defined compartments. The objective here is to see how well such a simplified model reproduces some of the qualitative features seen in Figure 1.

We consider a single human body in which heat transfer between the blood and the body tissue is dominated by convection through the rate of perfusion of the tissue. It is assumed that no heat losses take place between the outlet of the HLM and the aortic inlet of the patient. For simplicity we measure all temperatures in this model from a reference value of the normal blood temperature.

Let $f(t)$ be the temperature of the blood, which is determined by the HLM. Given the linear behaviour in the fall and rise of the core temperature seen in Figure 1, we define $f(t)$ by setting $f(0) = 0$ and

$$f'(t) = \begin{cases} -a, & 0 \leq t < t_1 \\ 0, & t_1 \leq t < t_2 \\ a, & t_2 \leq t < t_3, \end{cases} \tag{1}$$

where the cooling procedure commences at time $t = 0$, the main surgical procedure commences at $t = t_1$ (and the temperature is then kept constant), surgery finishes and the rewarming process is started at $t = t_2$, and the rewarming process finishes at $t = t_3$. Here a represents the rate of cooling and rewarming of the blood.

The temperature $T(t)$ in the tissue is then governed by

$$\frac{dT}{dt} = W^*(T)(f(t) - T) \tag{2}$$

where $W^*(T)$ is proportional to the perfusion rate of blood through the tissue.

We solve equation (2) with an initial tissue temperature $T(0) = T_0 < 0$. This matches the situation in Figure 1, where the peripheral temperature is initially below that of the core.

We have considered two scenarios for $W^*(T)$, namely

$$W^*(T) = W_0 \quad \text{and} \quad W^*(T) = W_0 e^{kT}, \tag{3}$$

where W_0 and k are both constants. This second scenario relates to the observations of Stolwijk [6] that the rate of perfusion of tissue varies with temperature as

$$W(T) \propto 2^{\frac{T - T_{ref}}{10}} \tag{4}$$

For simplicity we have thus assumed an exponential function to see what effect this has on the temperature distribution within the tissue.

In the case of $W^*(T) = W_0$ equation (2) reduces to

$$\frac{dT}{dt} = W_0(f(t) - T) \tag{5}$$

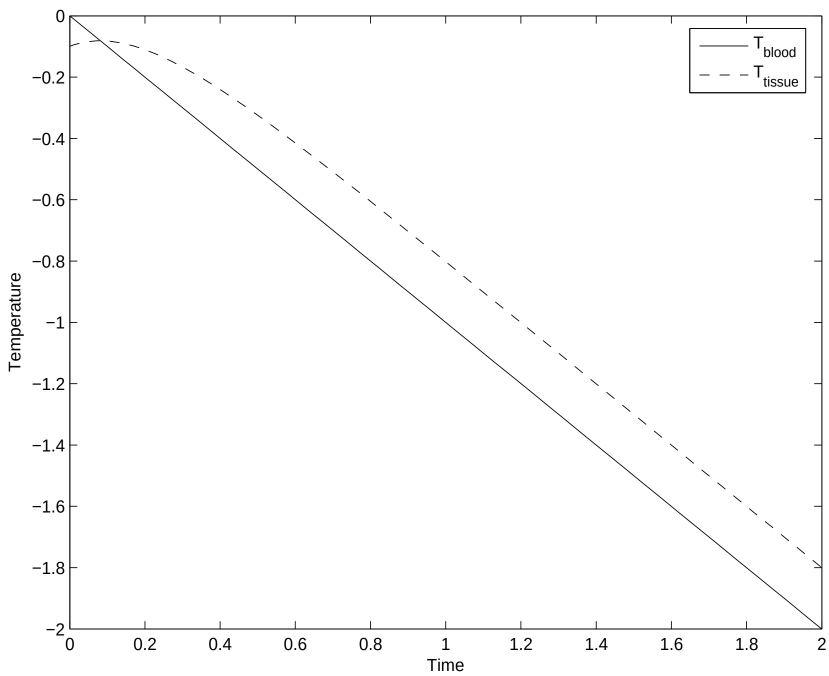


Figure 2: The effect of temperature reduction on the body tissue as predicted by the one compartment model. Here $W(T) = 5$ and $f'(t) = -1$.

which has an explicit solution. The part that is defined on $0 < t < t_1$ is

$$T(t) = -at + \frac{a}{W_0} + \Big(T_0 - \frac{a}{W_0}\Big)e^{-W_0 t} \qquad \text{for} \qquad 0 \leq t < t_1. \tag{6}$$

We note that for large t, $T(t) \rightarrow -a(t - \frac{1}{W_0})$. Hence the temperature decreases linearly, the difference between the blood and tissue temperature given by $\frac{a}{W_0}$. This is confirmed by a plot of the cooling part of the solution as shown in Figure 2. We note that although the model can reproduce the observed cross-over between blood and tissue temperature, the two curves remain parallel, given the linear dependence of T for long time-scales, and hence the two curves do not show the divergent behaviour evident in the cooling part of Figure 1.

We next include a temperature dependent perfusion rate to see if this produces any of the observed behaviour. In this second case of $W^*(T) = W_0 e^{kT}$ equation (2) is now given by

$$\frac{dT}{dt} = W_0 e^{kT}(f(t) - T), \tag{7}$$

where $f(t)$ is still given by equation (1). Figure 3 shows a numerical solution to this equation, again for the cooling part of the procedure. We note that this curve shows a more divergent behaviour between the temperature of the blood and that of the body tissue – a result which more closely resembles the behaviour shown in Figure 1.

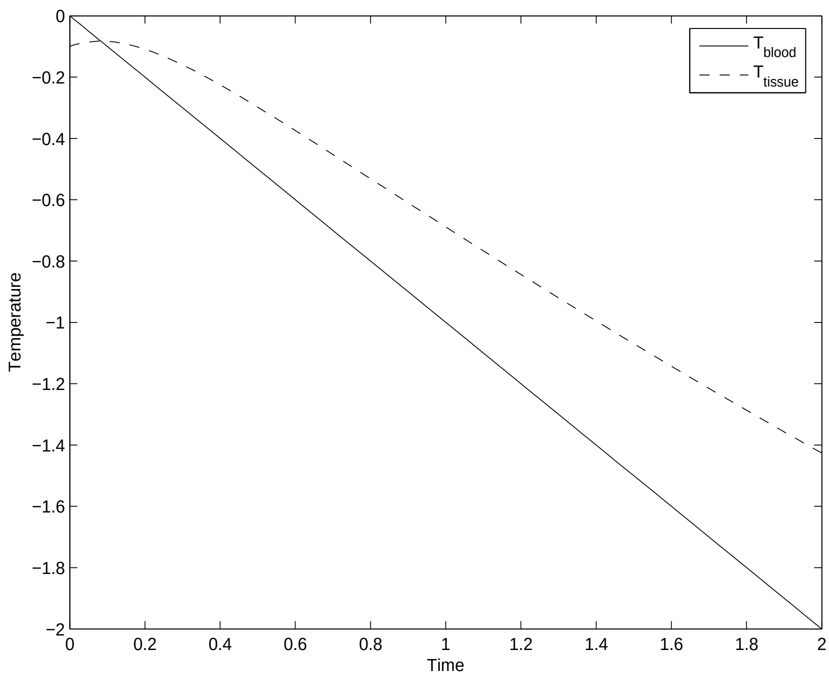


Figure 3: The effect of temperature reduction on the body tissue as predicted by the one compartment model. Here $W(T) = 5e^T$ and $f'(t) = -1$.

4 A three-compartment model – The 'Amsterdam' model

Whilst the simple one-compartment model formulated in the previous section has provided insight into the heat transfer process between the blood pool and the body tissue, we now turn our attention to the issue of understanding what causes afterdrop.

In order to do so we consider a three-compartment model consisting of a blood pool, rectal region (small and large intestines) and peripheral parts of the body. The blood pool is considered to be that of the core region of the body, whereby the heating of the core regions is assumed to be instantaneous. We further assume that heat transfer is dominated by the effects of perfusion of the blood through the rectal and peripheral compartments, except for the heat transport between the rectum and the periphery.

Whilst model data is available elsewhere in the literature for temperature recordings taken in other regions of the body, our focus here is on developing a model which accounts for temperatures recorded in both the nasal cavity, which we have taken to be part of the core, and the rectum. Given the low perfusion rate of the periphery, in particular fat, and its relatively high conductivity, the periphery may actually act as a heat source during the cooling procedure and a heat sink during rewarming of the body. Hence we include it here to see what effect it will have on the overall blood (core) temperature.

The equations governing the heat transfer process are given by

$$V_C\rho_C c_C\frac{dT_B}{dt} = \begin{cases} -a, & 0 \le t < t_1,\\ 0, & t_1 \le t < t_2,\\ a, & t_2 \le t < t_3,\\ -\rho_B c_B V_R W_R(T_B - T_R) \\ \qquad - \rho_B c_B V_P W_P(T_B - T_P), & t_3 \le t \le t_4, \end{cases} \quad (8)$$

$$V_R\rho_R c_R\frac{dT_R}{dt} = \rho_B c_B V_R W_R(T_B - T_R) - k_{RP}(T_R - T_P), \quad 0 \le t \le t_4, \quad (9)$$

$$V_P\rho_P c_P\frac{dT_P}{dt} = k_{RP}(T_R - T_P) + \rho_B c_B V_P W_P(T_B - T_P), \quad 0 \le t \le t_4, \quad (10)$$

where

- T_B, T_R and T_P are the temperatures of the blood, rectum and periphery;
- a is the rate of cooling and rewarming of the blood;
- W_R and W_P are the blood perfusion rates of the rectum and periphery;
- k_{RP} is the heat transport coefficient between the rectum and periphery;
- ρ_i and c_i $(i = B, C, R, P)$ represent the density and heat capacity of the blood, the core organs, the rectum, and the periphery; and
- V_i $(i = C, R, P)$ represent the volume of the core, rectum and periphery.

In comparison to the protocol discussed in Section 3 there is an additional period, $t_3 < t < t_4$, during which the HLM is switched off and the body regulates its own temperature via the heat balance of the fourth part of equation (8).

We see that in this final period the model confirms that the total heat content of the body

$$V_C\rho_C c_C T_C + V_R\rho_R c_R T_R + V_P\rho_P c_P T_P$$

is conserved.

We assume that all parts of the body are approximately at the same temperature at the start of the cooling procedure such that

$$T_B(0) = T_R(0) = T_P(0) = T_0. \quad (11)$$

Data from Fiala et al. [2] gives that the ratios of densities and heat capacities in the different regions are approximately equal to unity. Hence we can simplify the above model by dividing throughout by the respective $\rho_i c_i$ on the left-hand side of each equation to yield

$$V_C\frac{dT_B}{dt} = \begin{cases} -a^*, & 0 \le t < t_1,\\ 0, & t_1 \le t < t_2,\\ a^*, & t_2 \le t < t_3,\\ -W_R^*(T_B - T_R) - W_P^*(T_B - T_P) & t_3 \le t \le t_4, \end{cases} \quad (12)$$

$$V_R\frac{dT_R}{dt} = W_R^*(T_B - T_R) - k_{RP}^*(T_R - T_P) \quad 0 \le t \le t_4 \quad (13)$$

$$V_P\frac{dT_P}{dt} = k_{RP}^*(T_R - T_P) + W_P^*(T_B - T_P) \quad 0 \le t \le t_4, \quad (14)$$

where W_i^*, k_{RP}^* and a^* are rescaled perfusion, transport and cooling rates given by

$$W_R^* = V_R W_R, \quad W_P^* = V_P W_P, \quad k_{RP}^* = k_{RP}/(\rho c) \quad \text{and} \quad a^* = a/(\rho_C c_C).$$

The presence of the pre-factor of the different volumes for each region allows us to see what effect such regions, in particular the periphery, may have on the temperature of the blood and rectum.

4.1 Parameter Values

The model was solved for estimated values of the volume of the core, peripheral, and rectal regions and the change in blood temperature as dictated by the HLM. Here we have assumed that the volume of the periphery and core are approximately the same and that of the rectal region is considerably less, i.e.

$$V_C = 40l = V_P \text{ and } V_R = 10l. \tag{15}$$

We assume that the rate of perfusion of the rectum and the rescaled coefficient of heat transport between the rectum and the periphery are approximately equal and for simplicity take

$$W_R^* = 1/s = k_{RP}^*.$$

The perfusion rate of the periphery is considerably less, and we take $W_P^* = 1 \times 10^{-3}/s$.

4.2 Model solutions and results

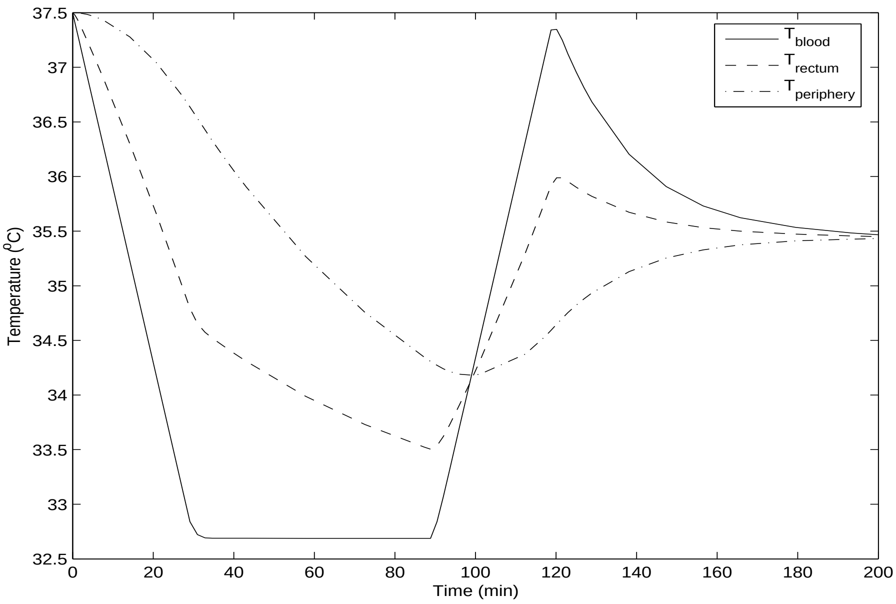
Equations (12)-(14) can be solved for a number of different scenarios, showing how the time length of each particular phase affects the heat distribution in the different regions.

We begin by considering a normal surgical procedure whereby the predicted temperature of the core, rectum, and periphery are shown in Figure 4(a). It is noted that the peripheral temperature drops at a much lower rate than that of the core and rectal temperature. This produces many of the qualitative features of the experimentally recorded temperatures shown in Figure 1. Here the afterdrop effect is quite considerable and the time taken for the three regions to reach an equilibrium temperature is relatively long.

Figure 4(b) shows the change in temperature in the three regions for a case in which the surgical procedure did not take place, i.e. some emergency may have interrupted the operation. Whilst the change in temperature between each of the three compartments is similar, the afterdrop in temperature is greatly reduced. This is because the periphery has not been allowed to cool for a long enough period; therefore during the rewarming procedure it is a reduced heat sink in comparison to the case of the normal surgical procedure.

The results of Figure 4(b) indicate that if the body can be re-warmed for a longer period of time then the effect of the peripheral and rectal regions acting as heat sinks could be reduced. In order to see whether this is the case we investigated holding the blood (core) temperature constant for a period following the rewarming process. The results for two different times (30 and 60 minutes respectively) of holding the

(a)



(b)

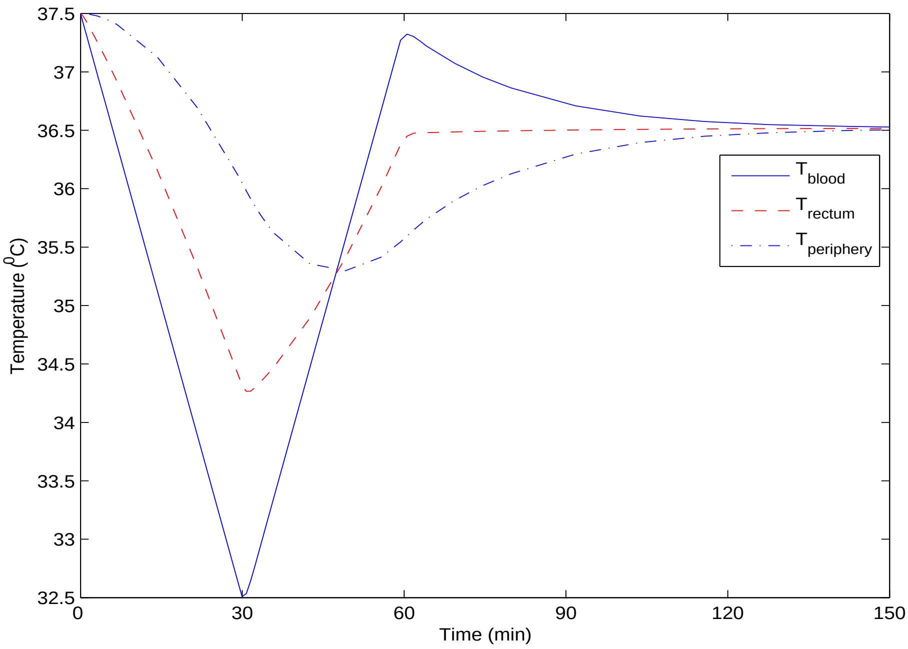


Figure 4: (a) The cooling and rewarming procedure for a surgical time of 60 minutes and (b) The effect of a short surgical time on the rewarming procedure. Note the small afterdrop in temperature.

temperature constant is shown in Figures 5(a) and (b). Here we note a significant reduction in afterdrop in each case whereby the 30 minute warming appears to halve the afterdrop effect and that of 60 minutes has a slightly greater effect.

5 Summary and discussion

We have formulated a number of models to understand cooling and rewarming of patients during cardiac surgery. A simple one-compartment model has reproduced some of the differences in qualitative behaviour between the core organ and peripheral (muscle, fat and skin) body regions. The assumption that the perfusion rate of the tissue is dependent upon the tissue temperature reproduced the correct behaviour in temperature change between the tissue and blood temperatures, specifically during the cooling process.

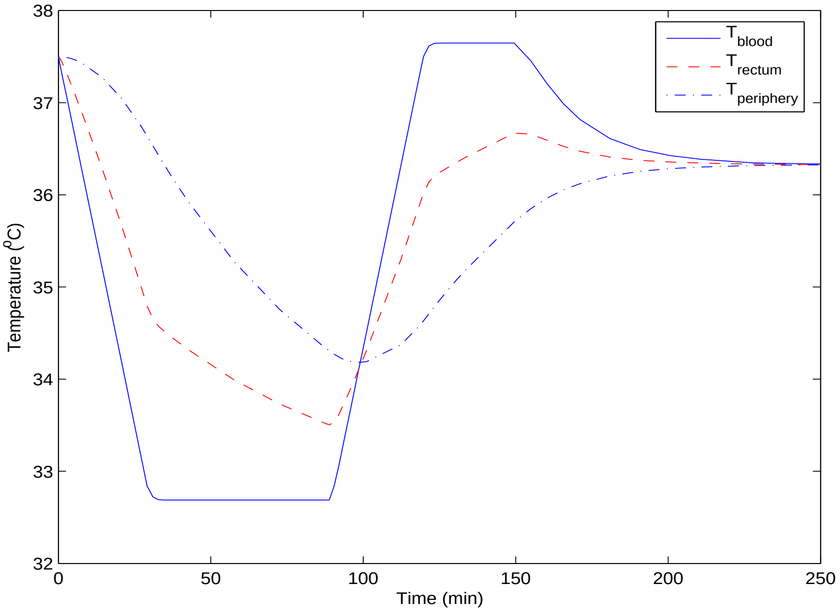
A three-compartment model was then formulated in order to understand the heat transfer process between the core organs, rectal region, and peripheral body parts and the effect that varying perfusion rates have. This model reproduced much of the observed behaviour in the temperature differences between each region and showed that a procedure of keeping the patient connected longer to the HLM at a high blood temperature, after the rewarming phase, has a considerable effect on reducing afterdrop. An initial analysis of the effect of excess body fat, i.e. fat versus thin people, on the rewarming procedure shows that fatter patients may not necessarily need to be rewarmed for longer given that the peripheral regions do not have enough time to drop to near the core temperature. However, this result appears to be at odds with clinical experience and requires further investigation. One effect that has not been considered in this model is that of the temperature-dependent rate of perfusion considered in the one-compartment model. This may have important consequences for the rewarming of the peripheral body regions.

The 'Amsterdam' model has helped answer a number of questions raised during the Study Group, in particular how temperature distribution varies throughout the different body regions and most importantly how the effect of afterdrop can be reduced.

Suggested areas of future work include:

- establishing the importance of metabolism and its possible role during rewarming;
- understanding the affect that excess body fat has on the re-warming process;
- experimental and clinical testing of the results of the Amsterdam model;
- assessing the effect of temperature-dependent perfusion on the Amsterdam model;
- accounting for the effects of thermal cooling and heating. The effect of the use of thermal blankets during or at the end of the surgical procedure has not been taken into account. This effect may have important consequences on some of the rewarming recommendations detailed above;
- heat losses, for instances large evaporative heat losses in the open thorax during surgery.

(a)



(b)

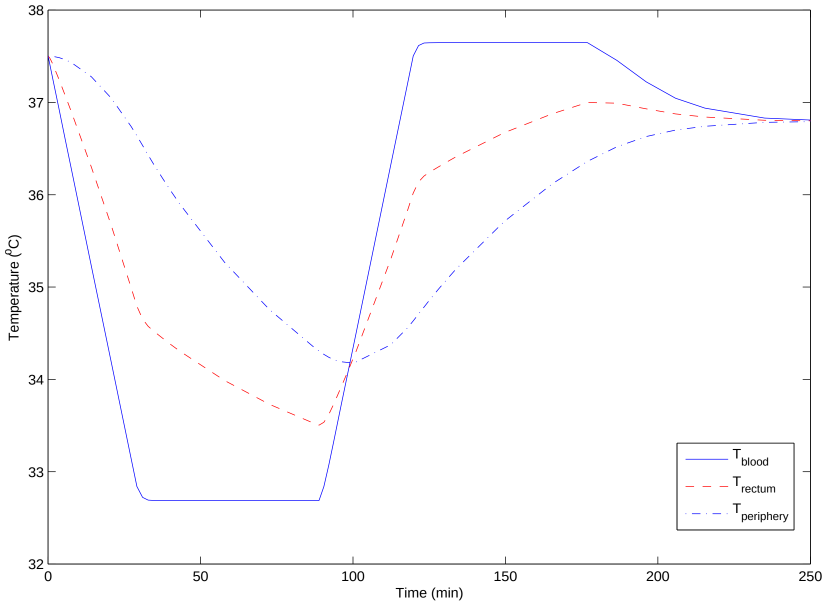


Figure 5: The effect of maintaining the core blood pool at a constant temperature at the end of the rewarming procedure using the HLM reduces the afterdrop effect. Here two cases are considered: (a) in which the core temperature is held constant for 30 minutes and (b) whereby the core temperature is held constant for 60 minutes.

Contributors

Dr. Joyce Aitchison (University of Oxford, UK), Dr. Christina Giannopapa (Technische Universiteit Eindhoven, Netherlands), Mr. Vincent Guyonne (Vrije Universiteit, Amsterdam, Netherlands), Mr. Miroslav Kramar (Vrije Universiteit, Amsterdam, Netherlands), Mr. Simon van Mourik (Universiteit Twente, Netherlands), Ms Jasmina Panovska (University of Edinburgh, UK), Dr. Mark Peletier (Technische Universiteit Eindhoven, Netherlands), Ms. Natascha Severens (Technische Universiteit Eindhoven & AMC, Amsterdam, Netherlands) and Dr. Marcus Tindall (University of Oxford, UK).

Acknowledgements

The Study Group participants are particularly grateful to Prof. dr. mr. Bas de Mol and his cardiac surgery team for allowing them to visit him in his surgery during surgical hours and for answering questions pertinent to the cooling and rewarming protocol.

References

[1] Analysis of Heat Exchange During Cooling and Rewarming in Cardiopulmonary Bypass Procedures, Curtis, R.M and Trezek, G.J. in *Heat Transfer in Medicine and Biology*, Shtizer, A. and Eberhard, R.C. (eds), 261-286., Plenum, New York, 1985.

[2] A Computer Model of Human Thermoregulation for a Wide Range of Environmental Conditions: the Passive System, Fiala, D., Lomas, K.J. and Stohrer, M. J. Appl. Physiol., 87 (5), 1957-1972, 1999.

[3] Computer Prediction of Human Thermoregulatory and Temperature Responses to a Wide Range of Environmental Conditions, Fiala, D., Lomas, K.J. and Stohrer, M. Int. J. Biometeorol. 45, 143-159, 2001.

[4] Analyis of Tissue and Arterial Blood Temperatures in the Resting Human Forearm, Pennes, H.H. J. Appl. Physiol., 1 (2), 93-122.

[5] Tissue Heat Content and Distribution During and After Cardiopulmonary Bypass at 17°C, Rajek, A., Lenhardt, R., Sessler, D.I., Grabenwöger, Kastner, J., Mares, P., Jantsch, U. and Gruber, E. Anesth. Analg., 88, 1220-5, 1999.

[6] A Mathematical Model of Physiological Temperature Regulation in Man, NASA contractor report CR-1855, NASA, Washington DC, 1971.