Modelling Heat Transfer in Humans

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Abstract

Temperature plays an important role in the functioning of biological systems. To predict tissue temperatures, the influence of blood flow must be accounted for. The collective effect of blood vessels in a tissue volume may be reasonably successfully described by a heatsink. This is for instance the case in our study of using scalp cooling to prevent hair loss induced by chemotherapy. In the calculation of overall temperature distributions the thermoregulatory mechanisms of vasoaction, sweating and shivering need to be considered. Models get increasingly sophisticated, but accurate predictions for individuals (rather than average behaviour) remain difficult because of the many influencing factors. A predictive tool for individual patients, including effect of anaesthesia, is being developed for use during hypothermic (cardiac) surgery.

1 Introduction

Temperature influences the functioning of biological (sub)systems. For humans, the core temperature varies within narrow bounds around about 37°C. Changes in temperature can have significant consequences for the behaviour of individual cells and the body as a whole. The temperature dependence of biological processes can be used to clinical effect. Examples are hyperthermia treatment against cancer; cooling of the head to prevent hair loss as a side effect of chemotherapy; and cooling of patients during major surgery to protect the brain. Intervention can also be necessary to maintain or restore normal temperature, e.g. during or after exposure to harsh environmental conditions. Conversely, the functioning of cells influences temperature and hence temperature measurements can be used in diagnosis. Mathematical models have a role both in treatment and diagnosis. They can aid in predicting the time course of temperatures or in giving information on the temperature where (invasive) thermometry is lacking.

Heat transfer within the body takes place by means of conduction and convection. Convective transfer by blood plays a key role. Problematically, densities of blood vessels are very high and hence it is hard to compute a detailed temperature distribution in even a small part of the body while accounting for all of the blood vessels individually. Fortunately, the effects of the blood vessels can be described collectively with some success. In 1948, Pennes [13] devised his bio heat equation, also known as heatsink equation, in which the effects of all vessels are lumped together:

$$\nabla k_{\text{tis}} \nabla T - W_{\text{b}} c_{\text{b}} \left(T - T_{\text{art}}\right) + M = c_{\text{tis}} \rho_{\text{tis}} \frac{\partial T}{\partial t} \qquad (1)$$

Here, k_{tis}, ρ_{tis} and c_{tis} are respectively the thermal conductivity, density and specific heat of the tissue. In the heatsink term, c_{b} is the specific heat of blood, W_{b} the volumetric blood perfusion of the tissue [kg m^{-3} s^{-1}], and T_{art} the temperature of the arterial blood entering the volume. Finally, M is the volumetric rate of (metabolic) heat generation [W m^{-3}]. The bio-heat equation (1) describes the blood to tissue heat transfer as if it all takes place in the capillaries: blood reaches the capillaries with the temperature of the major supply artery. Subsequently, in the returning veins heat transfer with the tissue is again assumed negligible. The bio-heat equation has established itself as the most used continuum description of tissue heat transfer. Relatively good accuracy is achieved for highly perfused tissue (such as brain) because at high perfusion a relatively large proportion of the blood-tissue heat transfer does take place in the smallest vessels. But of course, heat transfer between tissue and blood does take place in vessels of all sizes. Because of this, firstly, the optimum continuum description also includes terms qualitatively different to the heatsink (effective conductivity, directed perfusion), and, secondly, large blood vessels can cause significant temperature inhomogeneities unpredictable by any continuum model. Especially in local hyperthermia therapy these inhomogeneities are extremely relevant and much effort has been put in the development of accurate thermal models that account for individual vessels. Much effort is put in the development of accurate models to take those effects into account and they are recently reviewed in van Leeuwen and van Steenhoven [10]. Here we will focus on the more global models, using the Pennes bioheat equation.

2 Scalp cooling to prevent hair loss due to chemotherapy

Chemotherapy often makes cancer patients lose some or all of their hair. Although temporary, this hair loss is a much feared side effect of the therapy. Cooling the scalp during chemotherapy treatment can prevent or reduce hair loss (Protière, [14]) thanks to two mechanisms. The first is a reduction in skin blood flow during cooling, which reduces the delivery of the drugs. The second is slower cell metabolism due to the lower temperature, resulting in less susceptibility to the drug. The success of scalp cooling varies strongly (Grevelman, [4]) which can be attributed to a lack of insight in the temperature dependence of these mechanisms and resulting uncertainty over the best cooling protocol. This is compounded by possible local variations in skin temperature and blood flow during cooling. Hence, a computer model is being developed which will describe all aspects of scalp cooling. The model includes sub-models to describe drug transport, heat transfer and hair follicle damage. Experiments are being conducted to find the necessary physiological and biological relations (Janssen et al., [6]). With the model complete, it will be possible to optimize the design and cooling protocol of scalp coolers. Here we will show some intermediate results.

The numerical model describing heat transfer in the head uses the Pennes heatsink (although perfusion in this case raises temperatures) equation. It was shown before that temperatures in a cooled neonatal head predicted with the Pennes model agreed well with predictions made including detailed discrete vasculature (Van Leeuwen et al., [8]). The head is approximated by a sphere, with layers representing different media: brain, skull, fat, skin, and hair (van Lenthe et al., [11]). Normal temperature profiles were first calculated, with metabolism and perfusion fixed at their basic values (Janssen et al., [7]). Subsequently the head was cooled by addition of a cap that was continuously supplied with cooling fluid with a temperature of -8°C. The normal tissue temperatures were used as the reference temperatures in the temperature dependent metabolism and blood flow relations and new steady state solutions were calculated. For typical tissue characteristics and hair layer thickness (see Fig. 1) the skin temperature drops from 34°C to about 18°C. It was shown that the thicknesses and thermal conductivities of the fat and hair layers are the most important parameters that influence skin temperature and perfusion. A hair layer thickness of 2 mm instead of the basic 1 mm decreased the skin temperature drop by 3.5°C, while instead a 0.5 mm layer increased the temperature drop by 8.2°C. In the former case the perfusion was still one third of that without cooling, but in the latter case the perfusion was less than one seventh. For the clinic, this means that a good fit of the cap is essential.

The large variation in perfusion reduction suggests that temperature is a major factor determining the amount of drugs delivered to the hair follicles. The temperature/perfusion model provides the necessary boundary conditions for a physiology based Pharmacokinetic (PBPK) model (Gustafson et al., [5]). Accounting for perfusion and temperatures of the scalp skin, the total amount of drugs that are delivered to the hair follicles can be estimated. The subsequent relations between drug delivery, extra cellular concentration, temperature, and hair follicle damage will be experimentally determined in the near future. The combination of sub-models will result in a complete model that can help in optimizing scalp cooling for hair loss prevention.

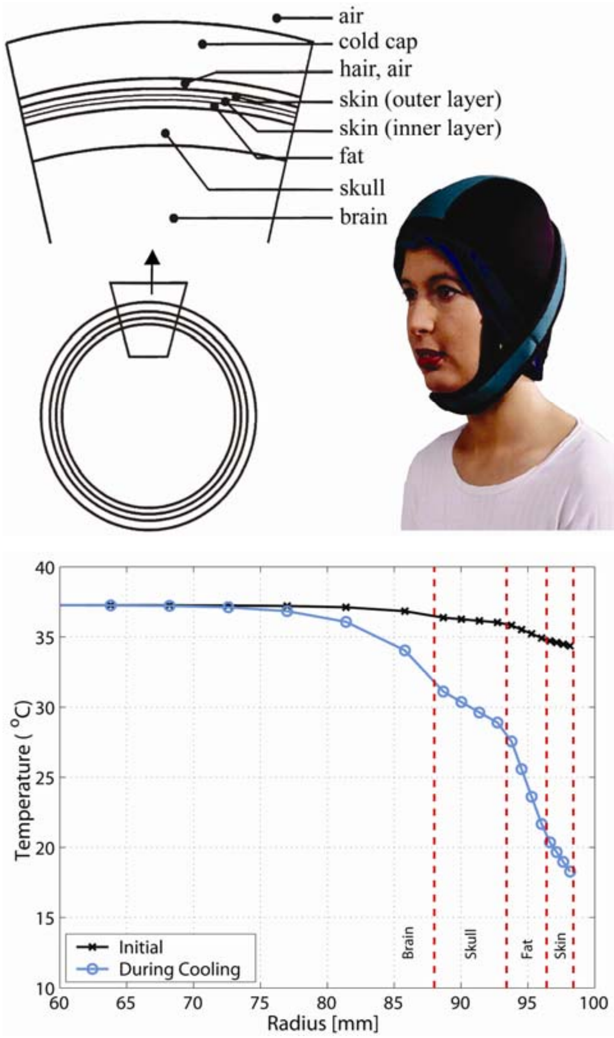


Figure 1: Upper left: configuration of the head model. Upper right: a typical scalp-cooling helmet. Down: temperature distribution in the head before and during cooling.

3 Human thermoregulation

The human body, when healthy, maintains its core temperature of about 37°C within small margins. The core consists of the brain and the internal organs in the trunk. Temperatures in the remaining parts of the body - `the periphery': surface tissue and the limbs - are much less constant. When environmental conditions vary, core temperature is maintained partly by behaviour (e.g. clothing), and partly by the body's thermoregulatory system.

Several models have been developed to describe whole-body heat transfer, from just two nodes describing core and periphery (e.g. Gagge et al., [3]) to multi-segment, multi-layered models. A recent model is that developed by Fiala et al. [1,2], which we adapted for our purposes (van Marken Lichtenbelt et al., [12]). The anatomy in Fiala's model consists of ten elements, see Fig 2, refining the earlier six segment model by Stolwijk [17]. Heat exchange with the environment takes place at the skin, and in the lungs/respiratory tract. The heat exchange by convection between skin or clothes surface and ambient air is described by a combined convection coefficient that considers both natural and forced convection. Also the heat losses due to radiation and evaporation are taken into account. Within the body, elements are made up of concentric tissue layers and heat transfer is modelled using the Pennes equation, with perfusions under control of the thermoregulatory system. By increasing or reducing blood flow to the skin, the body can increase or lower the skin temperature and hence its heat transfer to the environment. The thermoregulatory relations (Fiala et al., [2]) for blood flow, as well as those for shivering and sweating were found by using regression analysis on measured data from a large number of experiments.

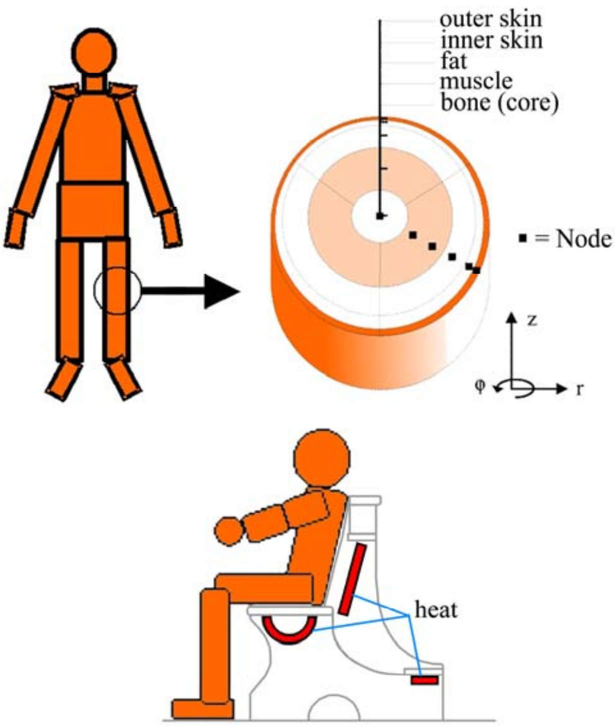


Figure 2: Top: Schematic representation of the model anatomy. The model is built from cylinders and a sphere for the head; the elements are divided in concentric layers and the layers, apart from the core are divided in sectors. Down: A schematic representation of the contact area of a person sitting on a pew with heat sources.

One informative use of the whole body model is the evaluation of different heating systems in monumental churches. Large temperature variations are damaging for the paintings, but high ceilings and poor insulation make the energy cost of constant heating in winter prohibitive. A possible way to save paintings and energy and still provide thermal comfort to churchgoers is by heating locally instead of heating the entire hall. This might be done by installing heating elements in the pews. In order for the heating system to work as effectively as possible experimental and numerical investigations are under way. The effect of radiative heaters in the pews is measured and calculated. A remarkable finding is the large influence of posture changes (sitting, standing) during the service.

4 Cardiac Surgery

Cooling is widely used to reduce metabolic demand and protect vital organs during open heart surgery. During cardiac surgery with cardiopulmonary bypass - the majority of cardiac surgical interventions - cooling is performed by means of the heart lung machine (HLM). The procedure consists of six distinct phases as detailed below:

1) The patient is anaesthetized. Due to anaesthetics the patient's metabolic rate is lowered and the threshold for vasoconstriction shifts to lower core temperatures. Furthermore the anaesthetics often contain vasodilatators. This leads to a lowering of the core temperature by approximately 2°C.
2) The first stage of the actual surgery: the thorax is opened.
3) The body is connected to a HLM which takes over the functions of heart and lungs. The HLM contains a heat-exchanger in which blood exchanges heat with water. In this stage the patient is cooled by adjusting the water temperature.
4) The main cardiac surgical procedure takes place and the body is kept at a constant low temperature. The temperature depends on the surgical intervention and can be near 30°C but also as low as 16-18°C.
5) On nearing completion of the surgical procedure the body is warmed at a steady rate by adjusting the water temperature of the heat exchanger. Rewarming must take place slowly in order to prevent cell damage. Because of their higher perfusion, core body parts (thorax and brain) react faster on rewarming than peripheral parts (arms and legs).
6) Once the core organs have reached the target temperature the patient is disconnected from the HLM and consequently control over the core temperature is relinquished. This often results in a phenomenon known as afterdrop: the core temperature temporarily drops. This effect is considered to be a result of the large temperature difference between the core and peripheral regions at the moment of decoupling (Sessler, [15]).

Patients who experience a large afterdrop need longer to recover and may experience more post-operative complications than patients who do not. Clinicians try to minimize the afterdrop as much as possible. Often forced-air heating blankets that are draped over the patient's legs are used in the rewarming phase. In this way the temperature gradient between the core and the periphery decreases. For the prevention of the afterdrop effect more knowledge about heat transfer in the anaesthetized human body during cardiac surgery is needed. We are building a numerical thermal model of the patient that can be used by clinicians to determine the optimal warming protocol in order to avoid afterdrop.

If the normal thermoregulatory model can be thought of to consist of two layers, describing respectively the physics of the system and the changes in this system by thermoregulation, then anaesthesia adds a third layer, describing the changes in thermoregulatory relations by anaesthetics and other drugs (van Leeuwen et al., [9]).

The most obvious change due to anaesthetics that should be implemented is a lowering of the thermoregulatory thresholds for vasoconstriction and shivering. Because a perioperative phase in which the effects of anaesthetics gradually wear off may need to be modelled, a variable was introduced that is a measure for the level of anaesthesia, Ca (0 < Ca < 1). There is currently only one variable Ca in the model, but it could be useful to consider using multiple anaesthetic variables in the case of multiple agents, and/or to have different Ca's for different tissue types in the body, reflecting different rates of uptake. Temperature shift parameters were introduced that shift the normal thermoregulatory thresholds. Because the thermoregulation should be the same as normal for Ca = 0, these shifts were made dependent on the depth of anaesthesia.

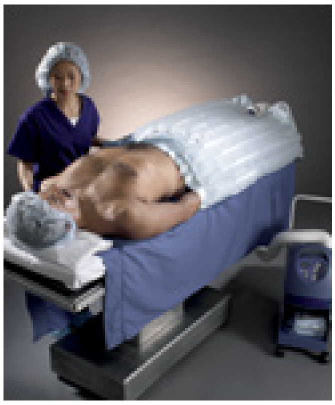
Apart from the anaesthesia, several particular conditions that are pertinent during (cardiac) surgery need to be accounted for in the computations. E.g. the open thorax and the immediate effect of heating blankets. With respect to the latter, the heat transfer coefficient of Bair Hugger blankets (Arizant Healthcare, Eden Prairie, MN, USA) was experimentally determined from measurements of the time evolution of the temperature of a solid aluminium cylinder wrapped in a Bair Hugger blanket.

Time [min]	Simulation
0-70	Supply anaesthetics: Ca=1, T_{room}=18°C, shivering prohibited
70-160	Cooling patient till 30°C, Ca=1, shivering prohibited
160-210	Rewarming till 37°C , using heating blanket, Ca=0
210-270	Decoupling from heart lung machine, using heating blanket, Ca=0

Table 1: Characteristics of the surgical procedure simulated with the model

With the 'in progress' model we simulated the temperature course during a cardiac operation (Severens et al., [16]). The procedure is characterized by the values in Table 1. In the simulation shivering is impaired during the first two phases. During the last two phases (t=160-270 min.) we assume that shivering is re-establishing. Also vasomotion is returning to a normal level. In Figure 3 the results for core and peripheral temperatures are shown. This result shows the main temperature characteristics as also observed in literature, like the slower reaction of the periphery compared to the core to the arterial blood temperature changes prescribed by the HLM and the characteristic afterdrop after decoupling the HLM.

Uncertainties in the model exist about the moment shivering actually starts and the chosen values in the vasomotion relations during surgery. Clinical data is now being collected to validate and refine the control equations - vasodilatation, vasoconstriction and shivering - for patients that undergo open heart surgery.



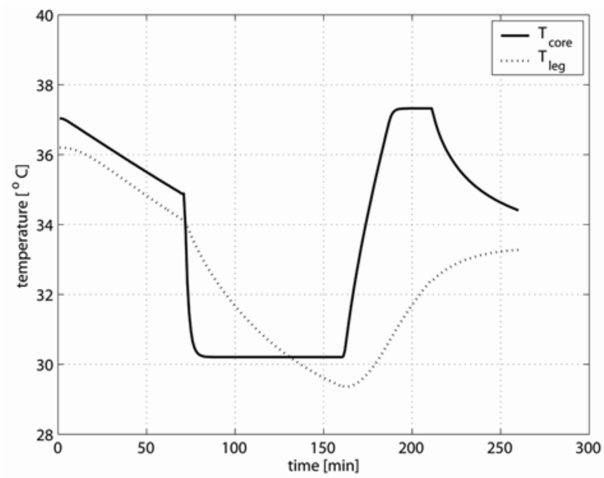


Figure 3: Core and peripheral temperature (down) computed for the operation with characteristics as in Table 1. Deep brain (solid line) and deep leg (dashed) temperatures are plotted. In the upper figure a typical heating blanket is shown.

4 Conclusion

Intricate biological and physical processes determine temperatures in humans. With the appropriate assumptions and simplifications usable predictions can be made. To make precise predictions for individuals in specific conditions extensive data acquisition is essential. For detailed temperature distributions this will include acquisition of tissue and vessel anatomy. For overall behaviour this could mean many individual parameters influencing thermoregulation.

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