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Simulation of scalp cooling by external devices for prevention of chemotherapy-induced alopecia

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ABSTRACT

Hypothermia of the scalp tissue during chemotherapy treatment (scalp cooling) has been shown to reduce or prevent chemotherapy-induced hair loss. In this study, numerical models are developed to investigate the interaction between different types of external scalp cooling devices and the human scalp tissue. This work focuses on improving methods of modeling scalp cooling devices as it relates specifically to the prevention of chemotherapy-induced alopecia. First, the cooling power needed for any type of device to achieve therapeutic levels of scalp hypothermia is investigated. Subsequently, two types of scalp cooling devices are simulated: a pre-cooled/frozen cap design and a liquid-cooled cap design. For an average patient, simulations show that 38.5 W of heat must be extracted from the scalp tissue for this therapy in order to cool the hair follicle to 22 °C. In practice, the cooling power must be greater than this amount to account for thermal losses of the device. Simulations show that pre-cooled and liquid-cooled cap designs result in different tissue temperatures over the course of the procedure. However, it is the temperature of the coolant that largely determines the resulting tissue temperature. Simulations confirm that the thermal resistance of the hair/air layer has a large impact on the resulting tissue temperatures. The results should be correlated with experimental data as an effort to determine the optimal parameter choices for this model.

1. Introduction

Hair loss, although not life threatening, is one of the most distressing side effects for patients undergoing chemotherapy treatment (Yeager and Olsen, 2011; Coates et al., 1983; Carelle et al., 2002). Scalp cooling was introduced in the 1970's as a method of reducing or preventing chemotherapy-induced alopecia (Dean et al., 1979). For this purpose, scalp hypothermia is generally achieved using cooling caps that fit over the patient's scalp. The cooling cap is applied prior to the beginning of chemotherapy drug infusion and cools the patient's scalp during the period of drug infusion. Generally, the cap is also worn for a period of time after infusion while the plasma concentration of the drug is still high. Temperature reduction has been shown to reduce hair loss by two mechanisms: vasoconstriction of blood vessels and reduced metabolic activity of hair follicle cells (Bulow et al., 1985). An early investigation found that patients who were cooled below 22 °C at a depth of 1–2 mm beneath the scalp surface showed better hair preservation (Gregory et al., 1982). This corresponded to less than 19 °C at the surface of the scalp (Bulow et al., 1985). While these values are commonly regarded as the optimal hypothermia conditions to prevent hair loss, this is not known precisely and relevant data is scarcely available (Breed, 2014).

In practice, the effectiveness of scalp cooling varies considerably due to a large number of factors; implementations of scalp cooling have differed in the type of cooling device, level of hypothermia, duration of hypothermia, and administered chemotherapy drug/dose. The type or design of the cooling device for this procedure is an important factor that has not been thoroughly studied (Breed et al., 2011). Over the years, various cooling cap devices have been developed to achieve this level of scalp hypothermia. One of the most common designs used currently is based upon a pre-cooled (frozen, cryogel-based) cap that is removed from a freezer and fitted over the scalp. Patients or nursing staff must exchange this type of cap (as it thaws) for a fresh, frozen cap several times during the scalp cooling procedure (Dougherty, 1996). Recently, more advanced (permanently-cooled) cooling devices have been developed that continuously cool the scalp using chilled fluid that flows through the cooling cap. The Paxman system is comprised of a refrigeration unit that circulates fluid with a temperature of −5°C through a light weight silicone cap (Massey, 2004). The Dignicap system is very similar to the Paxman system with the exception that the coolant is circulated at a

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temperature between 3 °C and 8 °C, normally set to about 5 °C (Ridderheim et al., 2003; Ekwall et al., 2013). As a first step, numerical models can be used to investigate the interaction between different types of external scalp cooling devices and the human scalp.

Several groups have put forth numerical models describing heat transfer within the human head (van Leeuwen et al., 2000; Nelson and Nunneley, 1998; Dennis et al., 2003; Xu et al., 1999; Neimark et al., 2008; Sukstanskii and Yablonskiy, 2007). Significantly fewer models exist to specifically describe heat transfer during scalp cooling for chemotherapy (Janssen et al., 2005a, 2005b). While the existing work provides detailed insight into important parameters in the scalp cooling procedure, little attention is given to the design of the scalp cooling device that is used for the procedure. The objective of this work is to investigate the influence of the design and operating parameters of the scalp cooling device used during chemotherapy. In order to achieve this objective, the methods used to model the cooling cap are considered in more detail than the previous models. Existing models utilize the same differential equation (namely the bio-heat equation) to govern heat transfer within the tissue and the cooling cap, which may lead to errors in accuracy. In this paper, the model is formulated using separate, coupled equations for the cap and the tissue. This formulation allows for a more detailed analysis of heat transfer within the cap, such as incorporating the effects of fluid flow for a liquid-cooled cap. Additionally, a model formulation is presented for a pre-cooled cap that accurately represents most pre-cooled caps that are currently used (i.e. not frozen due to the material composition of the coolant). Furthermore, previous models related to scalp cooling during chemotherapy used a 1-D formulation, thereby preventing them from being used to investigate cooling energy requirements. In this work, a 3-D, transient analysis of heat transfer is performed incorporating the effects of scalp cooling during chemotherapy. The cooling energy requirements for any type of scalp cooling device to achieve successful therapy are simulated. The influence of different types of external cooling caps is investigated by simulating the transient effects of these devices during chemotherapy treatment.

2. Methods

The heat transfer interaction between the human head tissue and a cooling cap can be modeled numerically. This physical system can be divided into two main parts for purposes of model formulation: the head tissue and the cooling cap (which extracts heat from the head tissue). Please refer to Appendix A for an explanation of symbols and abbreviations used in the development of this numerical model.

2.1. Model formulation – head tissue

The head geometry is created as a half-ellipsoid in 3-D space and is divided into different, homogenous layers: white matter, gray matter, skull, galea, hypodermis, dermis (inner), dermis (outer), and hair/air. A schematic of the layers of head tissue is shown in Fig. 1.

The overall dimensions of the head model are based upon small, medium and large head sizes from NIOSH Anthropometric Data and ISO Digital Headforms (Zhuang and Bradtmiller, 2005). A literature search was conducted to determine ranges and average values for thermo-physical properties of the tissue layers within the head. The selected thermo-physical properties reflect average values from these sources (Nelson and Nunneley, 1998; Dennis et al., 2003; Janssen et al., 2005a, 2005b; Fiala et al., 1999; Diao et al., 2003; Werner and Buse, 1988; Wilson and Spence, 1988; Torvi and Dale, 1994; Moreira-Gonzalez et al., 2006). A summary of the average thermal and physical properties of the human head tissue is shown in Table 1. Numerically, the hair/air layer is treated as a tissue layer with no blood flow or metabolic heat generation. Therefore, heat transfer within this layer is assumed to occur primarily by conduction. The dermal tissue is split into two layers similar to previous models (Fiala et al., 1999; Janssen et al., 2005b). The inner skin layer represents the cutaneous plexus and is highly perfused. The outer skin layer contains much smaller vessels with relatively little thermal significance.

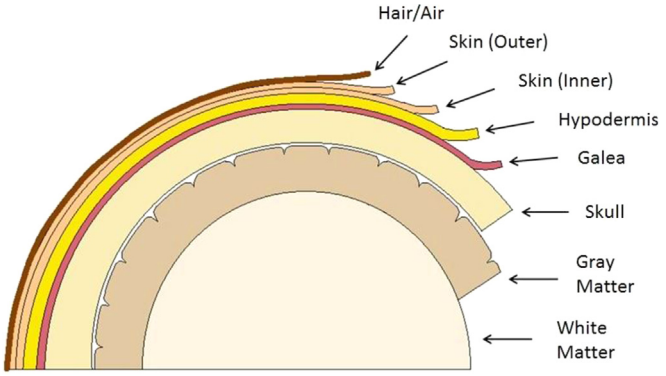

Fig. 1. Layers of tissue included in the human head model.

As in previous models, Pennes' bio-heat equation is utilized to govern heat transfer within the head tissue (Pennes, 1948).

$$\rho c\frac{\partial T}{\partial t}=\nabla\bullet k\nabla T+\rho_b c_b\omega_b\left(T_A-T\right)+q_m \tag{1}$$

where T is the tissue temperature, t the time, q_m the metabolic heat production, and T_A the temperature of the main supplying arteries. Here, k, ρ and c are the thermal conductivity, density and specific heat of the tissue, respectively. When accompanied by the subscript 'b', these symbols refer to the properties of the blood, instead of the tissue.

Hypothermia of the scalp tissue results in a reduction of cell metabolism, and therefore metabolic heat generation. The relationship between tissue temperature and cell metabolism can be described by the Q_{10} effect introduced by Van't Hoff. According to this formulation, the metabolism is reduced by a factor Q_{10} for every 10 °C change in tissue temperature. Values for the Q_{10} factor vary between 2.0 and 3.0 with a value of 2.5 assumed in this work (Dennis et al., 2003). The cellular metabolic heat generation is given as:

$$q_m = q_{m,0}\bullet Q_{10}^{\frac{T-T_0}{10\ ^\circ C}} \tag{2}$$

where T is the tissue temperature, and q_m the metabolic heat. When accompanied by the subscript '0', these symbols refer to the property in the thermoneutral state.

The skin tissue responds to hypothermia and reduced metabolic demand by reducing blood perfusion. Several models exist to describe the relationship between tissue temperature and blood perfusion. The Q_{10} effect can also be used to describe the change in skin blood perfusion (Stolwijk and Hardy, 1966).

$$\omega_b = \omega_{b,0}\bullet Q_{10}^{\frac{T-T_0}{10\ ^\circ C}}, \tag{3}$$

where T is the tissue temperature, and w_b is the blood perfusion of the tissue. When accompanied by the subscript '0', these symbols refer to the property in the thermo-neutral state.