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COOLING VIA HUMAN FOREARM FOR MULTIPLE SCLEROSIS

A-F. MAHROUS[1], S. MAHMOUD[2], R. K. AL-DADAH[3] & K. K. MATRAWY[4]

[1]Department of Mechanical Power Engineering, Menoufiya University, Shebin El-Kom, 32511, Egypt

[2,3]School of Mechanical Engineering, University of Birmingham, Birmingham, B15 2TT, UK

[4]Department of Mechanical Engineering, Faculty of Engineering, Assiut University, Egypt

ABSTRACT

The main objective of this research was to computationally investigate the effects of cooling via a human forearm on the tissue temperature for possible development in medical treatment of Multiple Sclerosis. A complete structure of a human forearm was modelled with CAD software and analysed using CFD to determine the temperature distribution through the forearm. Different cooling strategies were applied to human forearm including cooling the entire skin surface, cooling half the skin surface and use of Peltier coolers. The CFD results showed that cooling half the skin surface from bones side would be insignificant as the median nerve temperature was not considerably reduced by cooling. Cooling the entire skin surface, on the other hand, would result in lower median nerve temperature compared to other cooling scenarios. However, this might be worse for some people with MS symptoms. Proper selection of best cooling strategy would be based on people with MS symptoms experience.

KEYWORDS: Forearm Cooling, Multiple Sclerosis, Bio-Heat

INTRODUCTION

Multiple Sclerosis (MS) is a disease caused by the attack of the immune response on the central nervous system of a person. It was first identified in 1868 by Jean-Martin Charcot [1]. The term multiple sclerosis comes from sclerosis that means scarring and from multiple that relates to sites of scarring [2]. In the central nervous system, there are neurons that are full of axons which consequently are bounded by a substance known as myelin. The function of myelin is to deliver messages from the brain to other parts of the body, so that the human body responses and when damage occurs, MS takes place. This disease can occur at any age; however, it mainly occurs in young adults between the age of 20 to 40 and mostly in females.

Many individuals diagnosed with MS experience a temporary deterioration of symptoms when the heat or temperature in the body increases due to the surrounding conditions or physical activities. Symptoms for this disease such as fatigue, pain, tremor, muscle spasms, numbness, difficulty in moving, and visual problems are commonly worsened when the core body temperature increases [3]. Fortunately, MS is not fatal and the lifespan of the people with MS can be the same as a healthy person but it is a permanent condition. However, there is no known treatment for MS but a number of methods have proven effective in improving the disease. One of the beneficial methods is to extract heat from the entire body in order to reduce the overall tremor amplitude and frequency [4].

There is heat intolerance in MS that causes the patient to experience a symptom exacerbation due to heat exposure. Consequently, the ability of nerves to function decreases and heat slows down the nerve impulse transmission. The patient may recover from these symptoms when the body temperature goes back to the average temperature. The heat

intolerance can be severe as deaths were reported among the MS patients who were sunbathing or relaxing in hot tubs and this is probably due to the loss of ability to get rid of heat from the body. However, patients who are heat sensitive and develop symptoms quicker are also more responsive to cooling down and their symptoms will disappear quickly. Extraction of heat from the body would therefore help reduce the heat intolerance through a combination of decreased nerve conduction velocity, varied muscle properties and reduction of muscle spindle activity [5], thus improving the physical performance of the MS patients. By cooling the body, many people with MS experience relief from the unwanted symptoms.

A forearm is chosen to be the most appropriate and effective way for the heat extraction as it would not affect patient's daily activities when the cooling device is used [5]. The method of Cooling via Forearm for Intention Tremor in Multiple Sclerosis has been investigated in a number of publications. Feys et al. [4] investigated the effects of peripheral cooling on MS intention tremor symptoms. In such a study, a number of patients diagnosed with MS were selected to run the test and the mean age of these patients was 44.5 years, ranging from 18 to 63 years old. These patients were experimented with different temperature in a constant duration of time and then tests, such as finger tapping and wrist step tracking, were carried out before and after the cooling process so as to observe the difference in overall tremor amplitude and frequency. The study has shown a significant reduction in tremor amplitude after the cooling process. However, the main factors that caused the reduction were entirely unknown. Grahn et al. [5] believed that extracting heat from a human body through the palmar surfaces of a hand would be effective on reducing heat in the body of individuals diagnosed with MS. In this experiment, a chamber with an elastic sleeve was used for the heat extraction process by inserting one hand into it. Then, pressure and temperature were set to - 40 mm Hg sub atmospheric pressure and maintained at 18 to 22 ^{o}C, respectively. The results suggested that extracting heat from non-hairy skin surfaces could allow individuals diagnosed with MS to lengthen the duration of physical activities.

In the literature, an effort was made to model the temperature of human body [Huizenga et al. [6], Yildirim and Ozerdem [7], Miyanaga et al. [8], Wan and Fan [9], Shih et al. [10], Yang et al. [11], Rida et al. [12]]. Among them, Huizenga et al. [6] developed a model based on the Stolwjik model of human thermal regulation. There were four separated body layers for each body segment which are the core, muscle, fat and skin tissues in addition to a clothing layer. Factors such as metabolic heat production, sweating, vasodilatation and vasoconstriction were considered in the model. Heat transfer such as conduction, convection and radiation were treated independently due to other obstacles, since car seat and other external surfaces were also considered. The advantage of such model was the capability of predicting human physiological response to both non-uniform and transient thermal environments.

The main objective of this research was to investigate the effects of cooling via a human forearm on human body tissues temperature. A complete model of a human forearm was developed with Computer Aided Drawing (CAD) software and analysed by using Computational Fluid Dynamics (CFD) for the possible development in medical treatment of Multiple Sclerosis.

Bio-Heat Transfer Modelling of a Human Tissue

Normal human body is believed to be able to maintain a fixed body temperature of 37.0 °C. This is because humans are homoeothermic or endothermic which both means warm blooded living things that are able to uphold the body temperature constant. The main factors that are believed to be able to influence the core body temperature are age, diurnal, illness, metabolism rate, time of the day, sex, size and skin tone. As for metabolism rate, the higher it is, the higher the

average body temperature and vice versa. Whereas for time of the day, the average body temperature is more likely to be elevated at night and reduced in the morning. In order to normalize the human body temperature, a constant production of heat is needed and this comes from food consumed by the digestive system.

Physical laws of heat transfer, such as conduction, convection and radiation, control the heat transfer between the internal organs, body surface and the environment. The concentration of heat within the body is the factor that the heat constantly transfers from warmer to cooler areas; that is known as concentration gradient [13]. Factors such as blood perfusion rate, metabolism rate and thermal conductivity between internal body parts influence the rate of heat distribution over the entire body. Blood perfusion is the delivery of blood via blood vessels while metabolic heat generation is the heat generated through the metabolism process, both are temperature dependent and capable of affecting the thermal behaviour of living tissues. Various studies have produced several bio-heat transfer models that aim to quantify the problems mathematically (Wulff [14], Chen and Holmes [15], Song *et al.* [16] and Song *et al*. [17]), but they were complex and lacked sound experimental data to validate them (Liu [18]). With its simplicity and ability to accurately predict the temperature distribution in living tissues, the Pennes bio-heat equation (Pennes [19]) proved to be the best practical approach for modelling the bio-heat transfer behaviour. The general expression of Pennes bio-heat equation reads as

$$\rho c \frac{\partial T}{\partial t} = k\left(\frac{\partial^2 T}{\partial x^2} + \frac{\partial^2 T}{\partial y^2} + \frac{\partial^2 T}{\partial z^2}\right) + c_b w(T_a - T) + q \tag{1}$$

Where ρ, c, k, T, w, q, and t respectively are the density, specific heat capacity, thermal conductivity, temperature, blood perfusion rate and volumetric metabolic heat generation, and time. Subscripts a and b are for artery and blood respectively. The term on the left hand side of Equation (1) is the transient term, while the terms on the right hand side are the conduction, convection and metabolic heat generation, respectively. The well-known Q_{10} law relates the perfusion rate and metabolic heat generation with temperature. It states that, for every 10^{o}C reduction in tissue temperature, there is a corresponding reduction in cell metabolism and blood flow by the constant Q_{10}, which can be written as:

$$\frac{q}{q^o} = Q_{10}^{\frac{T-T_o}{10}} \tag{2}$$

$$\frac{w}{w^o} = Q_{10}^{\frac{T-T_o}{10}} \tag{3}$$

q^o and w^o are the metabolic heat generation and perfusion rate at a given temperature, T_o is the core temperature under normal conditions (37^{o}C), and Q_{10} is a constant with a value between 2.0 and 3.0. Diao *et al.* [20] used a Q_{10} of 3 and Janssen *et al.* [21] used a Q_{10} of 2.5. The presence of the Q_{10} Law amplifies the cooling effect. Apart from perfusion rate being dependent on temperature, past studies also suggested that perfusion rate is influenced by the brain condition. Diao *et al.* [20] suggested that the perfusion rate of an ischemic brain is only 20% of its normal value, and that the Q_{10} Law does not apply. Dennis *et al.* [22] echoed this suggestion by pointing out that the peak blood flow velocity to the brain is reduced to 10% of its normal value during severe stroke.

Due to the combination of disciplines in this area of study, many computational analyses were done by engineers with the medical researchers so as to further develop the investigation for the medical community as it is a part of the biomedical engineering field [23]. In this research, the Pennes bio-heat transfer equation was applied to create a User Defined Function (UDF) code to model the source term in energy equation, and then is used for the simulation of forearm cooling.

Geometric Modelling of Human Forearm and Conditions

The human forearm is considered as a part of the upper limb, located between the elbow and wrist. It is supported by two bones; the radius and ulna. There are two main arteries, two main veins and three nerves in the forearm. The two main arteries are known as the radial and ulnar arteries; their function is to carry oxygen rich blood out from the heart to the forearm. The two main veins involved in the forearm are deep and superficial veins. The function of deep vein is to go together with the deep arteries of the forearm, while superficial vein is used to go up in the subcutaneous tissue [24]. The three main nerves are the median, radial and ulnar nerves and each of them gets thicker as it goes up from the wrist to elbow. The major nerve of the anterior section of the forearm is the median nerve, which conducts impulses from the receptors of forearm to the brain and spinal cord to process and return the signals back to the forearm for a response [24].

The transformation of Computerised Tomography (CT) scans and Portable Network Graphics (PNG) files of human forearm was carried out by using the AMIRA software, version 5.0, to visualize 3D scans. The CT scans and MRI sections of forearm were received from the Department of Health and Human Services at the University of Birmingham [25]. The chosen scans were connected from the elbow to wrist to form the forearm model. The four sample scans shown in Figure 1 illustrates the first, second, third and fourth quarters of the entire forearm data set from the elbow to wrist, order is from top left to bottom right [25].

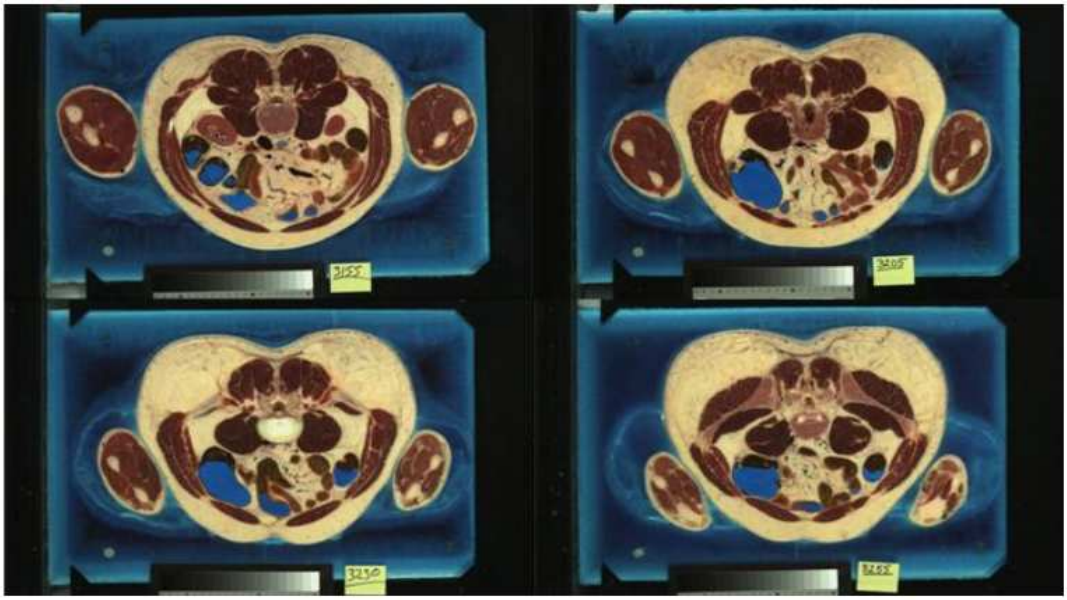

Figure 1: First, Second, Third and Fourth Quarters of the Entire Forearm Data Set [25]

Both Power SHAPE and Solid Works CAD software were used for the conversion of files and editing of model before exporting to the CFD code for simulation. The CFD code employed in this research was FLUENT 6.3. Due to the complexity of the slices, the forearm was divided into three parts, which were the skin, muscle and bones (Radius and Ulna). With the aim of making the forearm model more realistic, arteries, veins and nerves were included as those were one of the heat sources in a forearm. The major arteries, veins and nerves were constructed with Power SHAPE and placed into the final forearm model. Having the forearm model completed, the 3D model was exported to FLUENT pre-processor (GAMBIT). The model was divided into different volumes for meshing. The mesh density was about 1,370 cells/cm^3. Completely meshed forearm model, with Tetrahedral mesh elements, is shown in Figure 2 with different parts of human forearm. Second order discritization in momentum and energy equations was applied with SIMPLE algorithm as

pressure-velocity coupling. The temperature of blood was set as 36.8 ^{o}C. Material properties for both fluid and solid continuums were assigned as shown in Table 1.

The perfusion and metabolic heat generation terms of Pennes Bio-heat equation (Equation 1) are temperature dependent parameters, therefore a UDF code within Fluent was created and implemented to account for these relationships. With the physical and physiological properties of different tissues shown in Table 1, the developed model was used to investigate different cooling scenarios as illustrated in the next section.

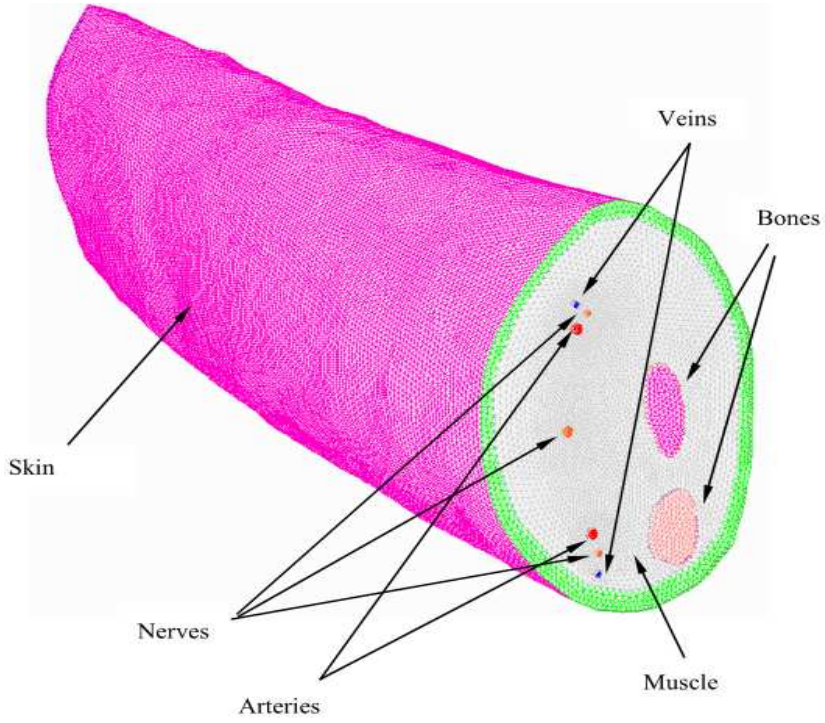

Figure 2: Mesh Configuration of 3D Forearm Model

Table 1: Physical Properties of Tissues Used in Modelling of Human Forearm

Forearm Components	Specific Heat Capacity, C ($Jkg^{-1}k^{-1}$)	Mass Density, P (Kgm^{-3})	Thermal Conductivity, K ($Wm^{-1}k^{-1}$)	Blood Perfusion, W ($Kgm^{-3}s^{-1}$)	Metabolic Rate, Q (Wm^{-3})
Skin	3570	1200	0.32	1.5	500
Muscle	3590	1060	0.39	2.38	500
Bones	1700	1500	1	0.15	130
Nerves	1676	1025	0.492	3.4	150
Arteries and Veins	1676	1025	0.492	19.5	150

RESULTS AND DISCUSSIONS

In this section, the CFD temperature distributions through different sections/parts of human forearm are investigated under different cooling strategies. To assess the CFD model for accurate prediction of temperature, the CFD results of present human forearm model were validated against data measured by Pennes [19]. The results are presented as temperature distribution along the transverse axis of the forearm. Tissue temperature versus depth curves of eight subjects (data points) together with CFD results, along the x=3mm line of the forearm mid section (left side of Figure 3), are shown

in Figure 3. The measurements were carried out by inserting Y-model thermocouples through the transverse axis of the forearm [19]. The normalized temperature in the vertical axis of Figure 4 is defined as:

$$Normalized\ Temperature = \frac{Tissue\ Local\ Temperature - Skin\ Temperature}{Maximum(Core)\ Temperature - Skin\ Temperature} \quad (4)$$

Whereas, the normalized radius in the x-axis of Figure 2 refers to the distance from the core of the forearm divided by half of the total transverse distance. As can be seen, good agreement between measured and CFD values is found with the maximum deviation being for subject 3 of the measured data. The CFD values are shown to lie completely within the domain of measurements for the eight subjects with acceptable prediction.

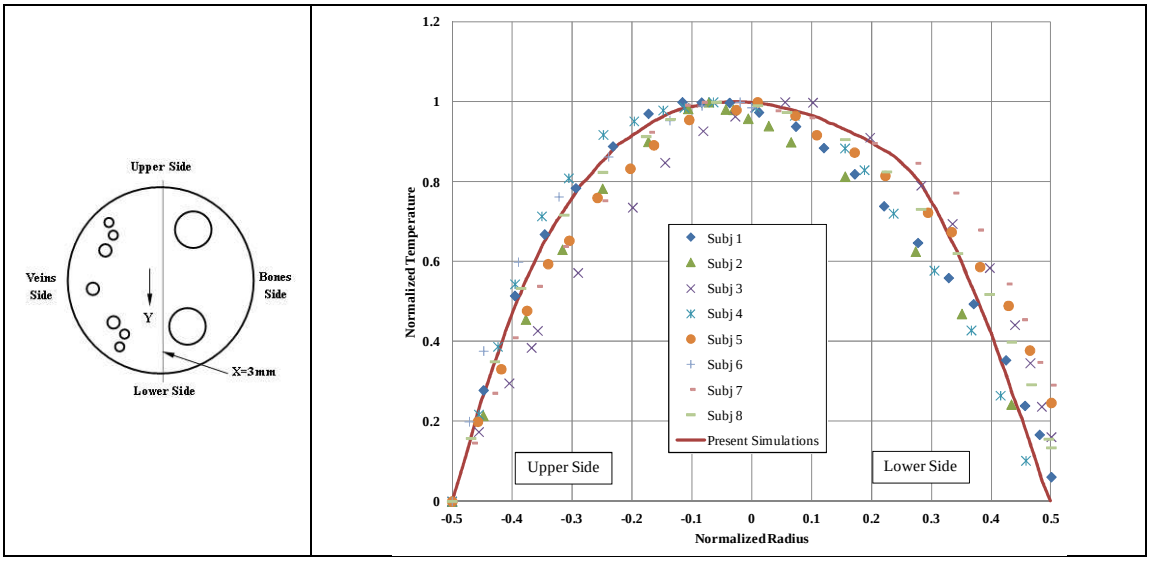

Figure 3: CFD Model Validation against Data Measured by Pennes [19]. CFD Temperature Distribution through Line X=3mm of the Simplified Mid Cross Section of the Forearm (Left Side)

Cooling the median nerve would probably result in decreasing the possibility of MS disease. Therefore the investigation focuses on how to reduce the temperature of median nerve by cooling the human forearm. For the purpose of MS, CFD simulations of forearm cooling were carried out under different cooling scenarios; these are:

- Cooling entire skin surface of human forearm at uniform skin temperature,
- Cooling half the skin surface of human forearm at uniform skin temperature, and
- Applying Peltier cooling to human forearm at localized regions.

The effect of cooling the entire human forearm at uniform skin surface temperature of 10^{o}C is shown in Figure 4. The temperature contours through lateral planes of the human forearm from elbow to wrist are presented in Figure 4a along with temperature distribution through the median nerve at the mid lateral section in Figure 4b. To keep the whole skin surface temperature at 10^{o}C, an equivalent cooling heat transfer rate of 18.05W is required. As illustrated in Figure 4a, the cooling effect uniformly takes place through the skin thickness and further through the muscle. This distance covers the region of nerves. The cooling effect becomes more effective at the wrist side where the thickness decreases. From Figure 4b, the average temperature of the median nerve at the mid lateral section is about 21.5^{o}C with a change in temperature through the nerve from core side to skin side of about 1.2^{o}C.

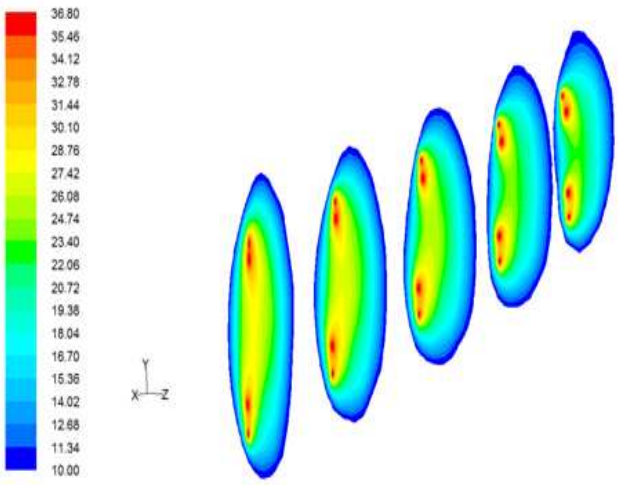

Figure 4a: Temperature Contours (In ^{O}c) Through Lateral Planes of Human Forearm When Cooling the Entire Skin Surface at Uniform Temperature of 10^{o}c

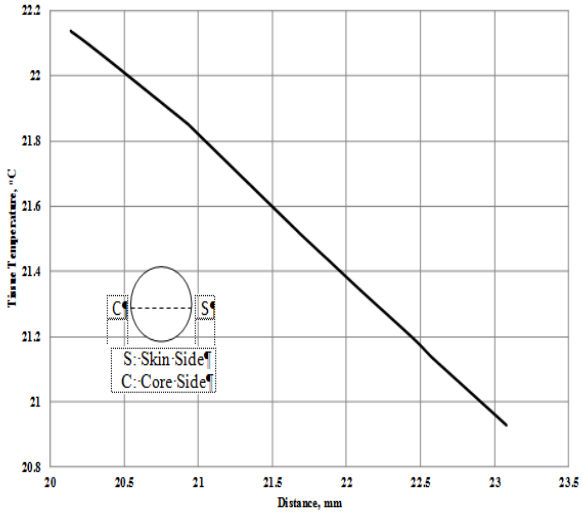

Figure 4b: Temperature Distribution throughout Median Nerve at Mid Lateral Section When Cooling the Entire Skin Surface at Uniform Temperature of 10^{o}c

The effect of cooling half the skin surface from veins, bones, upper and lower sides (see left side of Figure 3) are shown in Figure 5 (a, b, c and d), respectively. Cooled skin equivalent cooling heat rate is 16W when cooling from veins side and is 8.12W while cooling from bones side. On the other hand, cooled skin equivalent heat transfer rate is 10.87W for cooling from the upper side and is 12.71W when cooling from the lower side. When cooling half skin from veins side, the average nerve temperature is 24.2^{o}C; while it is 35.57^{o}C in case of cooling half skin surface from bones side. As illustrated, cooling half surface from the bones side (Figure 5b) is insignificant as the nerve temperature is not considerably affected by cooling. When cooling half skin surface, better cooling results would be obtained when cooling the skin from veins side with regard to nerve temperature.

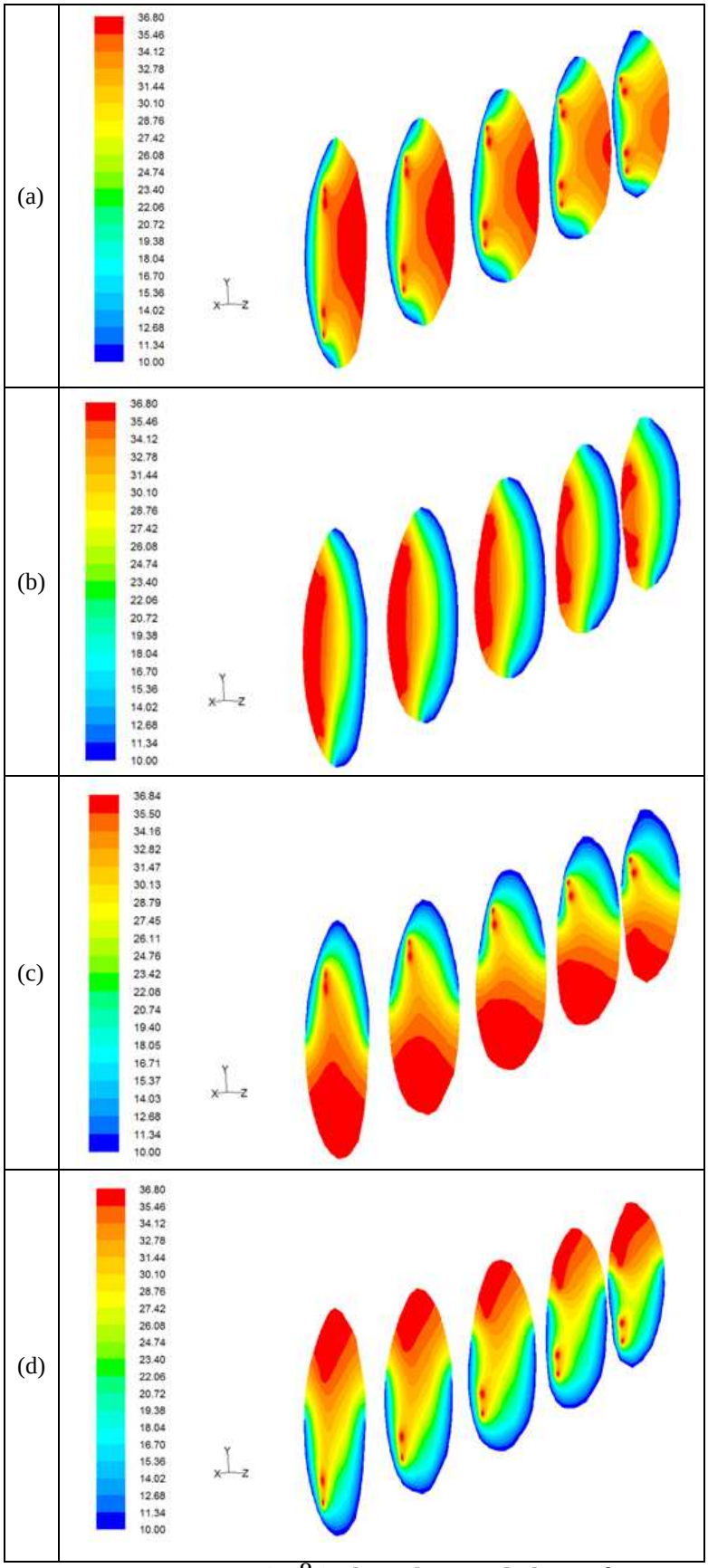

Figure 5: Temperature Contours (In ^{O}c) Through Lateral Planes of Human Forearm When Cooling Half Skin Surface at Uniform Skin Temperature of 10^{o}c (A) Viens Side, (B) Bones Side, (C) Upper Side, and (D) Lower Side

Another cooling strategy applied to the human forearm is the use of Peltier thermoelectric coolers at localized regions. Peltier cooler operates using the thermoelectric effect that take place between two junctions of dissimilar metals when voltage difference is applied. In a thermoelectric cooler, a large number of junctions are connected together in such a way that all cold junctions are connected on one side and all hot junctions are connected on the other side. The cold side is then attached to human forearm to get the necessary cooling effect. Figure 7 shows Peltier coolers on the model human forearm and also the possible investigated states for these coolers. The coolers may be positioned either on the UL-Position (State 1) or on the UR- Position (State 2). The un-cooled skin is computationally treated as adiabatic boundaries. For forearm cooling at State 1 (Figure 7a), a cooling rate of 12.44 W is required to keep skin spots at 10^{o}C; against a value of 11.86W for cooling at State 2 (Figure 7b). When compared to state 1, applying Peltier cooling at State 2 would result in a decrease in median nerve temperature.

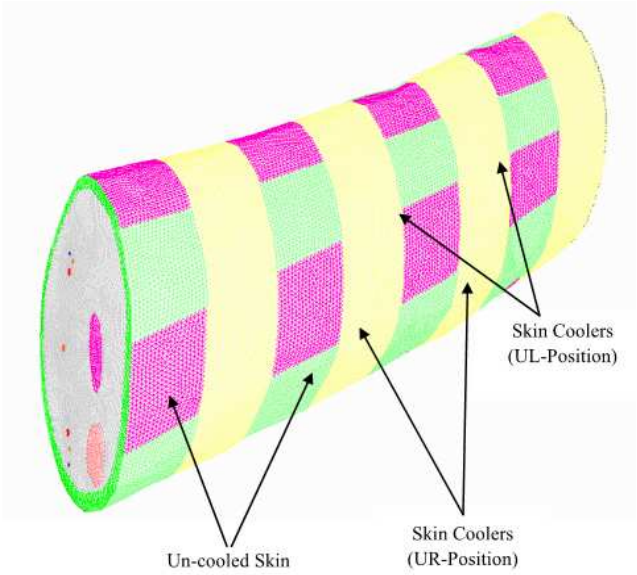

Figure 6: Peltier Coolers

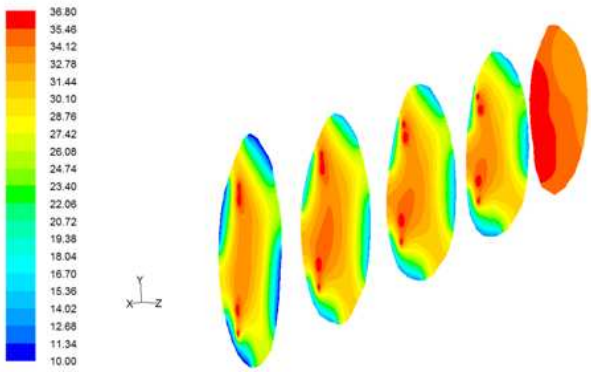

Figure 7a: Temperature Contours (In ^{O}c) Through Lateral Planes of Human Forearm with Peltier Coolers at UL-Position (State 1)

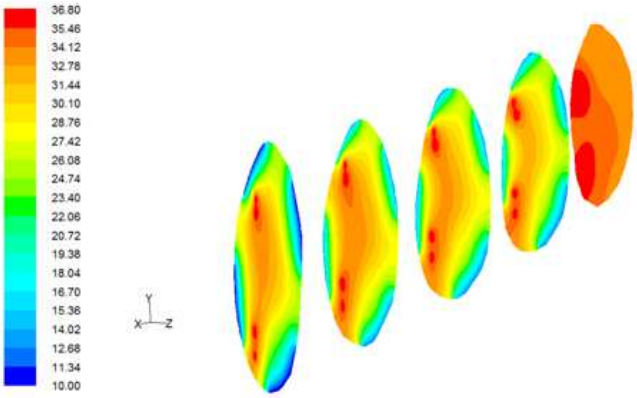

Figure 7b: Temperature Contours (In Oc) Through Lateral Planes of Human Forearm with Peltier Coolers at UR-Position (State 2)

Temperature distributions through the median nerve at mid lateral section of forearm are compared in Figure 8 for different cooling scenarios. From MS prospective, it is clear that cooling half the surface of the forearm skin from bones side would be insignificant as the median nerve temperature is not significantly affected by cooling. On the other hand, cooling the entire skin surface would result in lower median nerve temperature. However, such low median nerve temperature might have negative impact for some MS people, spasticity in particular [26].

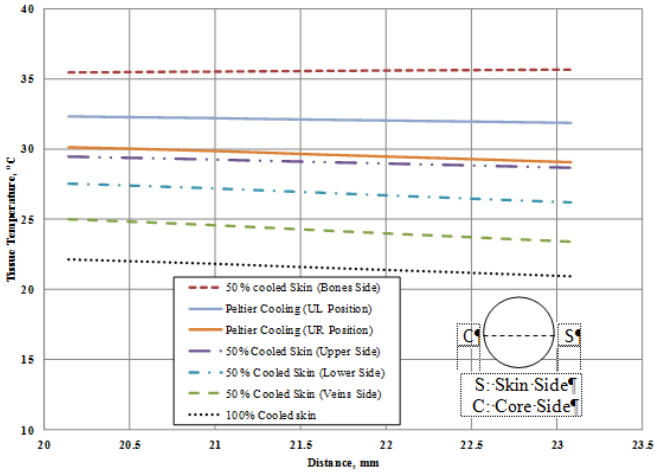

Figure 8: Comparisons of Temperature Distribution through Median Nerve at Mid Lateral Section for Different Cooling Scenarios

CONCLUSIONS

The effects of different cooling scenarios via a human forearm for the purpose of Multiple Sclerosis were computationally investigated. A complete structure of a human forearm was modelled using CAD software and analysed using CFD to determine the overall temperature. The cooling scenarios that were applied to human forearm model to reduce the possibility of having MS symptoms and consequently nerve damage are cooling the entire skin surface, cooling half skin surface and use of Peltier coolers. The results obtained showed that cooling the entire skin surface would result in lower median nerve temperature compared to other cooling scenarios. However, this might be worse for some people having MS symptoms. On the other hand, cooling half skin surface from bones side would be insignificant as the median nerve temperature is not considerably reduced by cooling. Most appropriate cooling strategy would be based on people with MS symptoms experience.

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