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Editorial

Journal of Biomechanical Engineering: Legacy Paper 2018

The *Journal of Biomechanical Engineering* has contributed to biomechanical engineering field since 1977. To honor papers published at least 30 years that have had a long-lasting impact on the field, the Editors now recognize "Legacy Papers." The journal is pleased to present the following paper as this year's Legacy Paper:

"A New Simplified Bioheat Equation for the Effect of Blood Flow on Local Average Tissue Temperature by S. Weinbaum and L. Jiji, ASME Journal of Biomechanical Engineering **107**: 131–139, 1985."

This paper has been cited nearly 500 times (Google Scholar) [1]. It provided a rigorous theoretical derivation of thermal effects of blood flow and blood perfusion in tissue, specifically to address limitations associated with the Pennes bioheat equation [2]. The paper energized the bioheat transfer community to seek an accurate yet simplified description of blood perfusion and incorporate it into a continuum model of heat transfer in tissue.

As heat transfer requires a temperature difference, it is essential to identify blood vessels with temperatures higher or lower than the temperature of their surrounding tissue. Until 1980, it was believed that, like gaseous (i.e., oxygen) transport, heat transfer takes place in the capillaries because of their large exchange surface area, implying that the temperature of the arterial blood does not change until the blood reaches the capillary. This concept was incorporated by Pennes when he developed his landmark Pennes bioheat equation in 1948 [2] which was more recently revisited by Wissler [3].

In the 1980s, several theoretical studies [4–6] were performed to illustrate how individual vessels participate in local heat transfer, and thus, to understand where the actual heat transfer between blood and tissue occurs. In these analyses, the concept of *thermal equilibration length* was introduced. The *thermal equilibration length* of an individual blood vessel was defined as a distance over which the temperature difference between blood and tissue drops to 1/e or 36.78% of the entry thermal difference value. Using this analysis, blood vessels smaller than 50 μm in diameter were predicted to quickly reach the tissue temperature suggesting all blood-tissue heat transfer must have already occurred before entering into the capillaries. On the other hand, for blood vessels larger than 300 μm in diameter, there is little change in blood temperature in the axial direction because their thermal equilibration length is much longer than their actual vessel length. This left medium-sized vessels between 50 and 300 μm in diameter to be defined as *thermally significant* because of their comparable thermal equilibration length and physical length. Indeed, these blood vessels were considered by this analysis to be primary contributors to tissue-blood heat transfer.

One of the contributions by Drs. Weinbaun and Jiji's research group was to appreciate the important thermal effect played by countercurrent heat exchange between large arteries and veins. It was observed that virtually all the thermally significant vessels ($> 50\,\mu$m in diameter) in the skeletal muscle were closely juxtaposed artery-vein pairs [6]. The countercurrent heat exchange mechanism, if dominant, was suggested as an energy conservation means since it provides a direct heat transfer path between the vessel pair. Therefore, it leads to a small thermal resistance between the warm artery and its countercurrent vein. Thermal equilibration in the artery (50–300 μm in diameter) in a countercurrent pair was estimated based on a simple heat conduction analysis in the cross-sectional plane. It was noted that the thermal equilibration length in the countercurrent artery was *at least three times shorter* than that in a single vessel of the same size embedded in a tissue cylinder [6]. A shorter thermal equilibration length indicates a smaller thermal resistance due to the shortcut of heat transfer pathway between the countercurrent artery and vein. Significantly shorter thermal equilibration length in comparison with that of a single vessel suggests that the primary blood tissue heat exchange mechanism for vessels larger than 50 μm in diameter in the deep layer is incomplete countercurrent heat exchange. Therefore, for modeling heat transfer in these tissue regions, reasonable assumptions related to the countercurrent heat exchange mechanism should be included to simplify the mathematical formulation. On the contrary, the original Pennes bioheat equation ignored the countercurrent heat exchange and it simply assumed that there is no driving force for heat transfer between the venous blood and tissue, thus, this assumption led to the completion of the Pennes perfusion source term in his 1948 paper.

The landmark 1985 paper by Weinbaun and Jiji intended to address the two major limitations of the Pennes model to improve accuracy in bioheat transfer modeling through what is now termed a "multiscale modeling approach" [1]. First, a microscale model based on the vascular structure in muscle, i.e., a countercurrent artery and vein arrangement for the thermally significant vessels larger than 50 μm in diameter, was constructed. Once there is a tissue temperature gradient along the countercurrent vessel axes, the artery and the vein transfer a different amount of energy across a plane perpendicular to their axes even if there is no net mass flow. This leads to a net energy transfer rate that is equivalent to an enhancement in tissue conductivity in the axial direction of the vessels. Detailed theoretical derivations were conducted to identify the equivalent thermal effect by the near-perfect countercurrent artery and vein heat exchange, and they found that the effect would lead to an enhancement in thermal conductivity in tissue. The derivations lead to the macroscale heat conduction model replacing the traditional tissue thermal conductivity with an expression of the enhanced thermal conductivity tensor (Eq. (36) in the paper). The tensor directly aligns with the directions of countercurrent vessel pairs relative to the local macroscopic tissue

temperature gradient. Based on the expression of enhancement in thermal conductivity in the simplified one-dimensional case, a large enhancement can be expected in large and closely juxtaposed blood vessel pairs ($> 50\,\mu$m in diameter) with high blood flow rate.

Both the Weinbaun-Jiji equation and the Pennes bioheat equation are continuum models that do not include individual blood vessels in the simulation domain, instead, the thermal effect of blood flow is incorporated into the traditional heat conduction equation via either adding a new term [2] or changing the values of some thermal properties [1]. Similar to the Pennes bioheat equation requiring the local blood perfusion rate to be known, the Weinbaum–Jiji model is simple to use as long as the enhancement in tissue thermal conductivity for the specific tissue region is given. Compared to a tissue region without considering blood flow, both equations are able to account for perfusion that would occur within realistic in vivo situations.

In the following decade after the publications of the 1985 paper by Drs. Weinbaum and Jiji, one saw many studies in the bioheat transfer community that sought better understanding of the thermal effect of vasculature and blood flow in in vivo tissue. Most of those studies were focused on evaluation of the assumptions introduced in the derivation of the Weinbaum–Jiji model, and experiments were designed to evaluate its accuracy in animal and clinical settings. This process and the ensuing communications among researchers in the bioheat transfer community led to a general consensus that a one-size-fits-all simple continuum model like the Pennes or the Weinbaum–Jiji equation is useful, however, the accuracy may suffer under conditions where the simplifications and assumptions used in their derivation are not strictly met.

The Pennes and Weinbaum–Jiji models represent two extreme situations of blood-vessel thermal interaction. In the original Pennes description, the arterial blood releases all of its heat to the surrounding tissue in the capillaries and there is no venous rewarming. In contrast, in the Weinbaum–Jiji equation, the partial countercurrent heat exchange is assumed to be the dominant mechanism for blood-tissue heat transfer. In other words, most of the heat lost by the artery is recaptured by its countercurrent vein rather than lost to the surrounding tissue. Several theoretical studies have suggested that one way to overcome the shortcomings of both models was to introduce a "correction coefficient" in the Pennes perfusion term [4,7–11]. In 1997, Weinbaum et al. modified the Pennes source term on the basis of the thermal analysis of a repeatable heat transfer unit of muscle tissue, a 1-mm-diameter tissue cylinder containing blood vessels smaller than $200\,\mu$m in diameter [9]. The countercurrent heat exchange between the supplying artery and vein defined in the anatomical studies of Myrhage and Eriksson in 1984 led to the estimation of the heat loss recaptured by the supplying vein [12]. The strength of the source term was then rederived taking into account the rewarming of the countercurrent venous blood in the tissue cylinder. This correction coefficient can be viewed as a weighting function to correct the overestimation of the original Pennes perfusion term. From the anatomic studies of the vascular arrangements of various skeletal muscles, the correction coefficient was found to vary from 0.6 to 0.8 under normal physiological conditions, indicating that there is probably a 20–40% rewarming of the countercurrent vein. Similarly, one earlier work by Baish generated vascular network following diffusion of angiogenic factors in tissue and showed that the Pennes perfusion source term overestimates the strength of heat released to or absorbed by local blood perfusion by approximately 20%, implying a correction coefficient of 0.8 [7]. In the meantime, other research groups also attempted to develop better models [13,14]. Unfortunately, these newly developed models still have "to-be-determined" parameters which require the development of a vasculature-tissue unit for establishing their relationship to the specific vasculature and blood perfusion rate.

Indeed, most of the newly developed bioheat models including the Weinbaum–Jiji 1985 paper are not regularly applied by bioengineering researchers due to the uncertainty of estimating the parameters such as the enhancement in tissue thermal conductivity and the correction coefficient. Thus despite its simplicity and shortcomings, the Pennes bioheat equation, which requires only a local perfusion rate and an arterial blood temperature as blood flow input, is relatively easy to use without detailed anatomical knowledge of the tissue vasculature. Furthermore, Tables of perfusion do exist in the literature for various tissues [15]. Currently, the thermal effects of small blood vessels between 50 and $300\,\mu$m in diameter are still normally modeled by the Pennes perfusion source term, with special treatments needed to address the impact of larger vessels. Indeed, the emphasis on bioheat transfer modeling has now shifted to model large individual blood vessels and their thermal interactions with the surrounding tissue and anatomy. This is facilitated by huge advancements in computational resources which allow the import of three-dimensional tissue geometry from MRI or CT imaging systems to commercially available numerical simulation software packages [16,17]. The dramatic increase in computer memory and calculating speed in the past decade enables the simulation of both steady-state and transient temperature distribution in three-dimensional tissue structures with embedded individual large blood vessels.

In conclusion, it is well accepted in the bioheat transfer community that the publication of the 1985 Weinbaum–Jiji model stimulated intense discussion and activity in the field. It prompted researchers to analyze the thermal effect of the vasculature in blood perfused tissue from a fundamental level. This was an early example of multiscale modeling to evaluate and simplify tissue anatomy and vasculature to create a continuum model of bioheat transfer. Although there is a continued desire to find a one-size-fits-all bioheat transfer model, these attempts generally suffer when the assumptions and simplifications of the model are not met, or the parameters needed are not known thereby reducing their accuracy. Improving model accuracy in bioheat transfer simulations may require modeling individual large blood vessels, which is only possible with the advancement in computational resources to handle vast data from scanned images of organs.

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