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Ilja L. Kruglikov

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Ilja L. Kruglikov
Wellcomet GmbH, Greschbachstrasse 2-4, 76229 Karlsruhe, Germany
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Temperature fields produced in the skin and adjacent subcutaneous white adipose tissue (sWAT) during and after exposure to ultrasound (US) waves are significantly dependent on the US frequency. In this study, we present theoretical descriptions of temperature fields appearing in composite skin/sWAT after exposure to US at frequencies of 3 MHz, 10 MHz, and 19 MHz. While the temperature increased by approximately 1.5°C in skin during US exposure at intensities up to 10.0 W/cm² and a frequency of 3 MHz, this increase reached 9.0°C and 16.0°C at US frequencies of 10 MHz and 19 MHz, respectively. Because of the large difference in heat capacitances and US attenuation coefficients in the skin and adjacent sWAT, the interface between these two layers was subjected to a temperature gradient that increased with US frequency. This gradient was low after applications of US at 3 MHz but was as high as 7.5°C/mm at 10 MHz and 14.0°C/mm at 19 MHz for US intensities of 10.0 W/cm². High temperature gradients produced by US at the dermis/sWAT interface can significantly affect the adherence between these two layers and thus modulate effective mechanical properties of the skin. © 2017 Author(s). All article content, except where otherwise noted, is licensed under a Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/). https://doi.org/10.1063/1.4997833

I. INTRODUCTION

Absorption of ultrasound (US) waves during their propagation in a homogeneous biological tissue causes temperature increase in the tissue, which exponentially decays with US penetration depth. Depending on the absolute value of the temperature increase, such heating can cause physiological reactions or morphological changes in the tissue. However, in inhomogeneous tissue, the attenuation of US is significantly dependent on the US frequency and on the microscopic tissue structure, especially at boundaries between single layers with different acoustic impedances.

Skin and adjacent subcutaneous white adipose tissue (sWAT) are two mutually confined layers with very different mechanical, thermal and acoustic properties and with distinct US attenuation coefficients. Mechanically, the bilayer skin/sWAT can be considered a composite with some adherence between the layers. Corresponding adherence strength is different in distinct facial fat compartments: adherence is weak in the medial and lateral midface, in some parts of the periorbital area, and in the temple, forehead, and neck. However, adherence is much stronger in the perioral and nasal facial compartments.

The skin/sWAT interface appears as a boundary between the dermis and sWAT with high and several times smaller US attenuation coefficients at the same frequency, respectively. Consequently, under suitable sonication conditions, cells located near this interface should be exposed to significant temperature gradients in a thin superficial layer of sWAT adjacent to the reticular dermis. This superficial sWAT layer is known as dermal (or interfacial) WAT. This layer contains adipocytes with transient phenotypes, which more readily undergo differentiation, hyperplasia, and

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E-mail: i.kruglikov@wellcomet.de
composite skin/sWAT, the following heat transfer equation is solved:

\[ \rho c_i \frac{\partial T_i}{\partial t} = k \nabla^2 T_i + Q_i - Q_{Pi} \]

where index \( i = s \) refers to the skin and \( i = a \) to the sWAT; \( T_i(x,t) \) is the temperature at depth \( x \); \( \rho_i \) is the mass density; \( c_{pi} \) is the specific heat capacity at constant pressure; \( k_i \) is the thermal conductivity; \( Q_i(x,t) \) is the distributed heat source due to US energy absorption; and \( Q_{Pi}(x,t) \) is the distributed heat sink from blood perfusion.

The distributed heat source \( Q_i(x,t) \) is due to US energy absorption in the tissue. For exponential US absorption, the distributed heat source is represented as

\[ Q_i(x,t) = I_0 e^{-\alpha_i t} \theta(\tau - t) \]

\[ Q_{Pi}(x,t) = I_0 e^{-\alpha_i f} h_d \alpha_a(f) e^{-\alpha_a(f)(x-h_a)} \theta(\tau - t) \]

where \( \alpha_i = \alpha_i(f) \) is the frequency-dependent attenuation coefficient of US; \( \tau \) is the duration of the US pulse; \( h_d \) is the dermis thickness; \( \theta(\tau - t) = 1 \) for \( 0 \leq t \leq \tau \), and \( \theta(\tau - t) = 0 \) for other \( \tau \). Generally, skin demonstrates different attenuation coefficients in the epidermis and upper and lower dermis; similarly, sWAT has superficial and deep layers known to have distinct mechanical properties. 

However, we first assume the skin and the sWAT as homogeneous layers having spatially constant thermal and mechanical characteristics.

II. THEORY

A. Bioheat transfer

Let \( x \) be the depth under skin, with \( x = 0 \) corresponding to the skin surface. A US wave at frequency \( f \) having energy density \( I_0 \) on the skin surface enters the skin perpendicular to its surface and penetrates the sWAT through the skin/sWAT interface, which is oriented parallel to the skin surface. The US beam is assumed to have a homogeneously distributed intensity over the radiating surface of the applicator. This simplification reduces the description of the temperature distribution and temperature gradients in the composite skin/sWAT to a one-dimensional problem.

US energy absorbed in the tissue is assumed immediately transformed into thermal energy causing a local temperature increase in the tissue. To describe the temperature evolution in the composite skin/sWAT, the following heat transfer equation is solved: 

\[ \rho_i c_i \frac{\partial T_i}{\partial t} = k \nabla^2 T_i + Q_i - Q_{Pi} \]

where index \( i = s \) refers to the skin and \( i = a \) to the sWAT; \( T_i(x,t) \) is the temperature at depth \( x \); \( \rho_i \) is the mass density; \( c_{pi} \) is the specific heat capacity at constant pressure; \( k_i \) is the thermal conductivity; \( Q_i(x,t) \) is the distributed heat source due to US energy absorption; and \( Q_{Pi}(x,t) \) is the distributed heat sink from blood perfusion.

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However, we first assume the skin and the sWAT as homogeneous layers having spatially constant thermal and mechanical characteristics.
The distributed heat sink \( Q_{Pi}(x, t) \) can be described by Pennes’ equation:

\[
Q_{Pi}(x, t) = c_b W(T - T_b)
\]

(4)

where index \( b \) refers to blood; and \( W(T) \) is the blood perfusion rate, which is strongly temperature-dependent. Furthermore, the following approximation for \( W(T) \) is used:

\[
W_s = W_{s0} \left\{ 1 + 9.2e^{-\left(\frac{T-44}{10}\right)^2} \right\}, \quad T \leq 44^\circ C, \quad W_s = 10.2W_{s0}, \quad T \geq 44^\circ C
\]

(5)

\[
W_a = W_{a0} \left\{ 1 + e^{-\left(\frac{T-45}{12}\right)^2} \right\}, \quad T \leq 45^\circ C, \quad W_a = 2W_{a0}, \quad T \geq 45^\circ C
\]

where \( W_{s0} = 0.45 \text{ kg/m}^3\text{s} \) and \( W_{a0} = 0.36 \text{ kg/m}^3\text{s} \) are normal blood perfusion rates in skin and sWAT, respectively.

Because the single tissue layers in the composite skin/sWAT have different acoustic impedances, US wave reflection on the skin/sWAT interface can reduce the energy penetrating the sWAT and thus, diminish the heating of the superficial sWAT layer. To estimate this effect, we consider the acoustic impedances, \( Z_i \), of the skin and sWAT, which are the products of their mass densities with corresponding US velocities. If a US wave of intensity \( I_0 \) falls perpendicular to the skin/sWAT interface, one part \( (I_{tr}) \) will be transmitted into the sWAT and another part \( (I_{ref}) \) will be reflected back into the dermis:

\[
\frac{I_{tr}}{I_0} = \frac{4Z_s Z_a}{(Z_s + Z_a)^2}, \quad \frac{I_{ref}}{I_0} = \frac{(Z_s - Z_a)^2}{(Z_s + Z_a)^2}, \quad I_{tr} + I_{ref} = I_0
\]

(6)

Acoustic impedances of the skin and sWAT were reported to be approximately \( Z_s = 1.99 \times 10^6 \) kg/sec/m\(^2\) and \( Z_a = 1.38 \times 10^6 \) kg/sec/m\(^2\), respectively.\(^{22}\) From (6), 96.7\% of US energy will be transmitted into the sWAT and only 3.3\% will be reflected on the interface skin/sWAT. Thus, at first approximation, we can neglect the reflection of US waves on this interface. We will also neglect reflections on sWAT/muscle and muscle/bone interfaces. This approach is a good approximation for sufficiently thick sWAT. We are primarily interested in the temperature increases in the skin and the skin/sWAT interface.

Temperature field calculations have been provided for the mass densities, heat capacities of the skin and sWAT\(^{23}\) and for the thermal conductivities of these tissues which are summarized in Table I.

To solve equation (1) and find the temperature distributions and gradients in the skin and sWAT for US waves of different frequencies, skin thickness and frequency-dependent US attenuation coefficients in both layers are required.

B. Variations of the facial dermis thickness

The absolute value of the dermis thickness \( h_d \) is dependent on the measurement procedure and is different in vitro and in vivo. This parameter has high inter-areal and inter-subject variations.\(^6\) Facial \( h_d \) shows strong spatial variations; dermal thickness is larger in the cheek and chin areas and smaller in the neck area.\(^{24}\) For example, \( h_d \) in the neck area has been reported to vary in the range 0.25-0.80 mm, in malar eminence area in the range 0.57-1.62 mm, and in the cheek area in the range 1.04-1.20 mm. In the non-wrinkled areas of human skin, \( h_d \) was 0.95 ± 0.28 mm with lower and upper limits of 0.35 mm and 1.65 mm, respectively.\(^{25}\) Due to this variability, \( h_d = 0.5 \text{ mm}, 1.00 \text{ mm}, \text{ and 1.5 mm} \) were used to model the influence of the skin thickness on the temperature distribution at the skin/sWAT interface.

**TABLE I.** Mass densities, heat capacities and thermal conductivities of the skin and sWAT.

| Tissue | Mass density, kg/m\(^3\) | Heat capacity, J/kg/K | Thermal conductivity, W/m/K |
|--------|---------------------------|------------------------|-----------------------------|
| Skin   | 1110                      | 3400                   | 0.4                         |
| sWAT   | 910                       | 2100                   | 0.2                         |
TABLE II. US attenuation coefficients in the skin and sWAT.

| US frequency, MHz | Attenuation in skin (neck), Np/cm | Attenuation in sWAT, Np/cm |
|-------------------|-----------------------------------|----------------------------|
| 3                 | 0.77                              | 0.26                       |
| 10                | 3.80                              | 0.79                       |
| 19                | 7.22                              | 1.26                       |

C. Attenuation coefficients of VHF-US in the skin and sWAT layers

While attenuation coefficients have demonstrated some temperature dependence, we will first consider the attenuation coefficients constant for all temperatures in this study.

1. Skin

The dependence of the attenuation coefficient $\alpha$ on 1-5 MHz frequency in human skin is described by the equation $\alpha_s(f) = \alpha_s(1)f^{0.6}$ where $\alpha_s(1) \approx 0.40$ Np/cm. The US attenuation coefficient at 3 MHz in skin can be assessed as $\alpha_s(3) \approx 0.77$ Np/cm. A frequency range of 10-25 MHz was investigated in Ref. 28, where attenuation curve slopes of 0.38 Np/cm/MHz and 0.43 Np/cm/MHz were reported for the neck and forearm, respectively. This corresponds to the following attenuation coefficients: $\alpha_s(10) \approx 3.80$ Np/cm and $\alpha_s(19) \approx 7.22$ Np/cm for the neck and $\alpha_s(10) \approx 4.30$ Np/cm and $\alpha_s(19) \approx 8.17$ Np/cm for the forearm. These values are in agreement with attenuation coefficients measured in porcine dermis at 20 MHz in vitro, i.e., $\alpha(20) \approx 8.2$ Np/cm. While the attenuation coefficient has been shown to be age and gender-dependent, we will also neglect these effects.

2. sWAT

The dependence of the attenuation coefficient $\alpha$ on 3-7 MHz frequency in human sWAT is described by the equation $\alpha_a(f) = 0.07f^{1.2}$ where $\alpha_a(3) \approx 0.26$ Np/cm. For 6-12 MHz, Nasief et al. reported on the frequency dependence of the attenuation coefficient as $\alpha_a(f) = 0.147f^{0.73}$ where $\alpha_a(10) \approx 0.79$ Np/cm. Assuming this dependence can be extrapolated to 19 MHz, the US attenuation coefficient at 19 MHz in sWAT was found to be $\alpha_a(19) \approx 1.26$ Np/cm.

Attenuation coefficients of the US in the skin and sWAT at three US frequencies considered in this study are summarized in Table II. These values were used for numerical solution of Eq. (1).

III. NUMERICAL MODELING

A. Method

Finite element analysis was applied to solve Eqs. (1)–(5). All simulations were performed with in-house code. This code was developed to simulate non-stationary problems of heat transfer in systems with non-linear, spatially distributed heat sources and spatially varying tissue properties. The code uses a fully implicit numerical scheme with a linear solver based on the TDM algorithm. The implemented algorithm can be applied to non-uniform meshes with arbitrary space discretization. In the present study, collocated meshes were used, i.e., the interface between different materials was assumed to be located between calculation nodes. The code was tested and verified against analytical solutions for uniform media for stationary and non-stationary cases.

In this study, the skin surface was assumed to be located at spatial coordinates equivalent to 0.0 mm. The calculated cell size in the skin layer was set constant at 5.0-10\(^{-5}\) m, whereas an exponentially increasing cell size was used for the mesh in the sWAT. Temporally and spatially dependent solutions for temperature and temperature gradients were obtained within the first 20 sec after US application with 0.01-sec steps for a 0-3 mm distance at 0.05-mm steps, respectively. Temperature fields were calculated as temperature differences from baseline, which was set for 36.6°C. Temperature gradients were calculated and are presented in °C/mm.

Calculations were performed at three US frequencies of 3 MHz, 10 MHz, and 19 MHz for three skin thicknesses of 0.5 mm, 1.0 mm, and 1.5 mm. Temperature fields for different frequency-thickness combinations were simulated at 10.0 J/cm\(^2\) for the following US application conditions: 1.0 W/cm\(^2\), 10 sec; 2.0 W/cm\(^2\), 5 sec; 3.0 W/cm\(^2\), 3.33 sec; and 10.0 W/cm\(^2\), 1 sec. To investigate the
influence of variable energy densities on the temperature fields, additional simulations were provided for all frequency-thickness combinations at 1.0 W/cm\(^2\) and application times of 7.5 sec and 15.0 sec. All simulations were performed with and without blood perfusion. To confirm the stability of the simulation results with varying skin thermal conductivity, two additional calculations with thermal conductivities 25% lower and higher than the average value (see Table I) were performed on skin with thickness 1 mm at 19 MHz, 2.0 W/cm\(^2\), and 5 sec.

The results of each simulation are presented as video clips demonstrating the temporal evolution of temperature and the temperature gradients over 20 sec and up to a 3 mm depth under the skin surface (up to 1,000 frames per clip). We determined the maximum temperature and temperature gradients for each given set of treatment parameters and calculated the corresponding two-dimensional spatial-temporal fields.

B. Temperature fields in the composite skin/sWAT at different US frequencies

Temperature fields and temperature gradients in a composite skin/sWAT having a skin thickness of 1.0 mm after US application at 1.0 W/cm\(^2\) for 10 sec and at 10.0 W/cm\(^2\) for 1 sec at different US frequencies of 3 MHz, 10 MHz and 19 MHz are presented in Fig. 1. US of 3 MHz produced low temperature increases in skin of approximately 1.5\(^\circ\)C. Temperature gradients at the skin/sWAT interface at 3 MHz were low at intensities up to 10 W/cm\(^2\). US applications at 10 MHz and 19 MHz and intensities 1.0 W/cm\(^2\) to 10.0 W/cm\(^2\) increased skin temperature by approximately 5.0-9.0\(^\circ\)C and 8.0-16.0\(^\circ\)C and skin/sWAT interface temperature gradients by 3-7.5\(^\circ\)C/mm and 5.0-14.0\(^\circ\)C/mm, respectively.

Fig. 2 shows the temperature fields and temperature gradients in the composite skin/sWAT after application of US at 10 MHz and 19 MHz and at the same energy density of 10.0 J/cm\(^2\) for different application times of 3.33-10 sec. The maximum temperatures and temperature gradients
FIG. 2. Temperature fields and temperature gradients in the composite skin/sW AT after application of US at the same energy density of 10.0 J/cm\(^2\) by different energy delivery rates of 1.0 W/cm\(^2\), 10 sec; 2.0 W/cm\(^2\), 5 sec; 3.0 W/cm\(^2\), 3.33 sec): a,b – 10 MHz; c,d – 19 MHz; a,c – temperature fields; b,d - temperature gradients.

significantly varied with sonication time. At the skin/sW AT interface, these parameters can reach 5.5°C and 5.0°C/mm (Fig. 2 a,b) and 7.0°C and 8.5°C/mm (Fig. 2 c,d) at 10 MHz and 19 MHz, respectively.

The temperature fields and temperature gradients in the composite skin/sW AT after US application at 2.0 W/cm\(^2\) and 5 sec and 10 MHz and 19 MHz for different skin thicknesses of 0.5 mm, 1.0 mm, and 1.5 mm are shown in Fig. 3. While variations in skin thickness for facial skin typically range from 0.5-1.5 mm and thereby affect temperatures in the dermis, the temperature gradient at the skin/sW AT interface is nearly the same for all thicknesses but strongly increase with increasing US frequency.

Fig. 4 shows the influence of the total US energy density on the temperature field. As the energy density increased from 10.0 J/cm\(^2\) to 15.0 J/cm\(^2\) at 10 MHz and 19 MHz and at 1 W/cm\(^2\), the temperature in the dermis significantly increased. However, only moderate temperature gradient changes were observed at skin/sW AT interface.

C. Influence of thermal conductivities on the temperature gradient at the interface skin/sWAT

Based on the calculations thus far, the thermal conductivities of the skin and sWAT were observed to be 0.4 W/m/K and 0.2 W/m/K, respectively (Table I), which corresponded with those reported elsewhere.\(^{34,35}\) The thermal conductivities showed significant variations dependent on temperature\(^{19}\) and water and collagen contents in tissue. For example, to describe heat transfer in the composite skin/sWAT, the following values were used by different authors for skin and sWAT, respectively: 0.445 and 0.185 W/m/K,\(^{36,37}\) 0.34 and 0.22 W/m/K,\(^{21}\) and 0.53 and 0.16 W/m/K.\(^{38}\)

Because variations in the skin and sWAT thermal conductivity can influence the development of temperature gradients at the interface between these layers, we calculated the temperature distribution and gradients at three skin thermal conductivities \(k_s = 0.3\) W/m/K, 0.4 W/m/K, and 0.5 W/m/K and
FIG. 3. Temperature fields and temperature gradients in the composite skin/sWAT with different skin thicknesses after US application at 2.0 W/cm$^2$ for 5 sec: a,c,e – 10 MHz; b,d,f – 19 MHz; a,b – 0.5 mm; c,d – 1.0 mm; e,f – 1.5 mm.

at constant sWAT thermal conductivity $k_a = 0.2$ W/m/K. The results are presented in Fig. 5. Variations in the skin thermal conductivity only slightly influenced the composite skin/sWAT temperature fields.

D. Spatiotemporal distributions of temperature and temperature gradients in the composite skin/sWAT

The spatiotemporal distributions of temperature and temperature gradients in the composite skin/sWAT with a skin thickness of 1.0 mm after application of VHF-US at 10 MHz and 19 MHz are presented in Fig. 6. The maximum temperature gradient was localized near the surface skin/sWAT and temporally corresponded with the US exposure time. This gradient quickly reduced with increasing distance from the interface.

A spatiotemporal analysis of the temperature demonstrated a relatively slow decay of the dermis temperature with significant heating of the skin at least during the time corresponding to two times that of US exposure.

IV. DISCUSSION

The dermal-sWAT interface plays an important role in affecting the mechanical properties of skin. Cells located in this area demonstrate strong reactions to different physical factors, such as mechanical stress and heat, and can undergo trans-differentiation, which can significantly modulate
FIG. 4. Temperature fields and temperature gradients in the composite skin/sWAT after application of US at different frequencies and energy densities: a,b – 10 MHz; c,d – 19 MHz; a,c – 10.0 J/cm$^2$; b,d – 15.0 J/cm$^2$.

the local mechanical parameters of composite skin/sWAT.$^{1–4}$ Moreover, the effective mechanical properties of the composite are significantly dependent on adherence between the two layers. Stronger adherence more effectively increases the influence of sWAT in determining the mechanical properties of the skin by decreasing the effective Young’s modulus of the composite and thus, increasing the susceptibility of the skin to the onset of structural instabilities typical for aging skin.$^{1}$ The ability to control adherence should be considered as an important tool in anti-aging strategies, and local heating of the interfacial area can sufficiently modify this property of composite skin/sWAT.

Modification of the structural and mechanical properties of the dermis-sWAT interface can be achieved by sufficient heating. The incorporated energy should be primarily absorbed within the vicinity of the interface. We recently showed that sufficient energy levels can be achieved by applying radio-frequency currents using optimally placed electrodes on the skin surface.$^{5}$ In the present study, we investigated whether similar effects could be achieved using very high frequency US waves.

FIG. 5. Temperature fields and temperature gradients in the composite skin/sWAT with skin thickness of 1 mm for different thermal conductivities of the skin after application of US at 19 MHz, 2.0 W/cm$^2$, 5 sec: a – temperatures; b – temperature gradients.
Temperature fields produced in the composite skin/sWAT under US exposure were significantly dependent on the US frequency. Whereas the application of 3 MHz US did not produce any substantial thermal effect in single layers or at the skin/sWAT interface, 10 MHz and 19 MHz provided significant local heating in the dermis, which remained at elevated temperatures beyond the period of US exposure. Approximately 17.3%, 31.6%, and 43.4% of US energy at 10 MHz and 30.3%, 51.4%,
and 66.1% at 19 MHz US energy were absorbed in skin of thicknesses 0.5 mm, 1.0 mm, and 1.5 mm, respectively. Thus, the application of 19 MHz US provided much stronger dermis heating with temperatures reaching 53°C at a US intensity of 10.0 W/cm².

Because of large differences in thermal conductivities and US attenuation coefficients in the skin and sWAT, the interface between these two layers experiences temperature gradients. At 19 MHz, this temperature gradient was approximately 5.0°C/mm and 14.0°C/mm at US intensities of 1.0 W/cm² and 10.0 W/cm², respectively. Corresponding temperature gradients were significantly lower at 10 MHz, reaching 2.5°C/mm and 7.0°C/mm, respectively. Temperature gradients after US exposure reached maximum values at the skin/sWAT interface and quickly reduced with increasing distance from the skin/sWAT interface.

The application of 19 MHz VHF-US to heat the dermis and produce high temperature gradients at the skin/sWAT interface could be utilized in the treatment of different dermatological conditions and aesthetic issues of normal skin thicknesses. The application of 10 MHz US could be beneficial for treating the skin/sWAT interface for very thick skins with thicknesses of more than 2.0 mm. These differences should be taken into account when developing dermatological treatments based on the application of very high frequency US waves.

V. CONCLUSIONS

Temperature fields produced in composite skin/sWAT during and after exposure to VHF-US were strongly dependent on the US frequency. At a US intensity of 10.0 W/cm², maximum temperatures in the dermis reached approximately 46°C and 53°C at US frequencies of 10 MHz and 19 MHz, respectively. These temperature fields were spatially inhomogeneous and characterized by high temperature gradients near the skin/sWAT interface, reaching 7.5°C/mm at 10 MHz and 14.0°C/mm at 19 MHz. These temperature gradients can significantly affect adherence between the skin and sWAT and thus modulate the effective mechanical properties of skin.

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