Use thermophysical property to quantify state of HIFU treatment for VLS

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Abstract. The aim of this study is to evaluate the performance of ADT methods in grading the effectiveness of HIFU treatment for VLS. High-intensity focused ultrasound has been identified as a promising treatment modality for vulvar lichen sclerosus, a common inflammatory disorder associated with an increased risk of developing vulvar carcinoma. With small probe on extensive VLS parts, the therapy was sometimes uneven, thus the total doses of HIFU machine couldn't indicate the curative effect at each part. The current therapeutic effect was based on symptoms and skin appearance after 3 months, which was time-consuming. Until now, there has been no immediate quantitative assessment method of HIFU therapeutic response for VLS. In our study, active dynamic IR thermal (ADT) was scheduled to undergo HIFU therapy before and after treatment. The thermal time constant was calculated based on ADT images measured both before and after HIFU treatment. In the result of pig phantom measurements, with each part approximately the same thermal time constant before HIFU treatment, the change of thermal time constant was strictly positively associated with HIFU dose onto each part. This study demonstrates the clinical potential of ADT in fast and effective quantify state of HIFU treatment for VLS.

1 Introduction

The radical cure of VLS is still lacking [1]. The current treatment for VLS focuses on symptomatic relief [1]. High-intensity focused ultrasound (HIFU) causes a sufficient rise in temperature[2, 3]. By improving microcycle, HIFU could benefit VLS symptomatically [4]. The working mechanisms of HIFU therapy has two categories: mechanical effects and thermal effects [5, 6]. Different from those use for the ablation of solid tumors [7], HIFU use for VLS is softer and avoid cavitation [4, 8].

The most common VLS occurs when the inflammation is intense enough to cause separation of a large area of skin [4]. The main mechanisms of HIFU treatment for VLS are thermal effects causing temperature increase of the vulva skin [5, 6]. To quantify the effectiveness of HIFU treatment dose of each point, we suggest to use thermophysical property values in active dynamic thermal imaging to evaluate the HIFU treatment therapeutic response of each target area. Ice packs were intermittently applied on affected skin for post HIFU treatment for VLS. Active dynamic IR thermal (ADT) imaging shows changes of thermal tissue properties [9]. Thus, ADT can be used for quantitative objective assessment of HIFU treatment efficacy.

However, the therapeutic assessment methods in these reports were based on symptoms and skin appearance, which were time-consuming (usually more than 3 months) and subjective. Until now, there has been no quantitative assessment method of HIFU therapeutic response for VLS.

This study demonstrates the clinical potential of ADT in fast and effective quantify state of HIFU treatment for VLS to evaluate the performance of ADT methods in grading the effectiveness of HIFU treatment for VLS.

2 Methods and Materials

It has been widely accepted that burn injury is dependent on exposure duration to the heat source and exposure power. Henriques [10] utilized an Arrhenius equation to describe damage of the tissues:

$$\omega = Aexp\left(-\frac{E}{RT}\right) \tag{1}$$

ω is the reaction rate, A is frequency factor, E is activation energy, R is universal gas factor and T is temperature. The total degree of tissue injury Ω is the integration of ω:

$$\Omega = A\int_0^t exp\left(-\frac{E}{RT}\right)dt \tag{2}$$

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Since the skin treated by HIFU suffers some kind of burn injury, the variation of thermal properties can be implemented to quantify how well the treatment is. In our case, we first exert cold excitation to the target area, and then remove cold source and have the skin self-warm up. The advantage of taking this method to determine burn level is that such procedure is a routine in HIFU therapy of VLS, therefore no redundant steps are added during curing. The general governing equation for heat transfer of this process is described by Pennes equation [11]:

$$\frac{\partial T(x,t)}{\partial t} = \nabla(k\nabla T) + q_s + q_p + q_m \tag{3}$$

In our case, we used the simplified equation which assuming [12]:

1. The temperature is only a function of depth and time.
2. Heat convection to the air is negligible.
3. Material constants are uniform in time and space.
4. Before removing the cold source, a linear temperature profile is assumed at the skin surface.
5. The temperature of depth d maintains constant.

Then, the equation is simplified as:

$$\frac{\partial T(x,t)}{\partial t} = \frac{k}{\rho c}\frac{\partial^2 T}{\partial x^2} \tag{4}$$

with the boundary condition:

$$T(x,0) = T_0 - T_s\left(1 - \frac{x}{d}\right), where\ t = 0, x \leq d \tag{5}$$

$$T(d,t) = T_0, where\ t \geq 0 \tag{6}$$

$$\frac{\partial T}{\partial x}(0,t) = 0, \text{where } t \geq 0 \tag{7}$$

To solve it, let:

$$\hat{T}(x,t) = T(x,t) - T_0 \tag{8}$$

Then the equations become:

$$\frac{\partial \hat{T}(x,t)}{\partial t} = \frac{k}{\rho c}\frac{\partial^2 \hat{T}}{\partial x^2} \tag{9}$$

$$\hat{T}(x,0) = -T_s\left(1 - \frac{x}{d}\right), where\ t = 0, x \leq d \tag{10}$$

$$\hat{T}(d,t) = 0, where\ t \geq 0\ \omega = Aexp\left(-\frac{E}{RT}\right) \tag{11}$$

$$\frac{\partial \hat{T}}{\partial x}(0,t) = 0, \text{where } t \geq 0 \tag{12}$$

Let:

$$\hat{T} = u(x)v(t) \tag{13}$$

$$\frac{k}{\rho c} = \alpha \tag{14}$$

By the separation of variables, *u* and *v* satisfy:

$$u''(x) = \frac{\lambda}{\alpha}u(x) \tag{15}$$

$$u'(0) = 0 \tag{16}$$

$$u(d) = 0 \tag{17}$$

and

$$v'(t) = \lambda v(t) \tag{18}$$

where λ is the eigenvalue for both differential equations. By solving it, we have,

$$u(x) = cos\left(\frac{(2n+1)\pi}{2d}x\right), n = 0,1,2 \ldots \tag{19}$$

$$v(t) = C_n e^{\lambda_n t}, where\ \lambda_\mathrm{n} = -\frac{(2n+1)^2\pi^2\alpha}{4d^2} \tag{20}$$

Let:

$$e_n = e^{-\frac{(2n+1)^2\pi^2\frac{k}{\rho c}}{4d^2}t} cos\left(\frac{(2n+1)\pi}{2d}x\right) \tag{21}$$

So

$$T(x,t) = T_0 + \sum_{n=0}^{\infty} C_n e_n \tag{22}$$

Combining the boundary condition and using inverse Fourier transformation, we finally obtain:

$$T(x,t) = T_0 - \frac{8T_S}{\pi^2}\sum_{n=0}^{\infty}\frac{1}{(2n+1)^2}e_n \tag{23}$$

We used the first three term of the series.

$$T(0,t) = T_0 - \frac{8T_S}{\pi^2}\left(e^{-\frac{t}{\tau}} + \frac{1}{9}e^{-\frac{9t}{\tau}} + \frac{1}{25}e^{-\frac{25t}{\tau}}\right) \tag{24}$$

where

$$\tau = \frac{4d^2\rho c}{\pi^2 \mathrm{k}} \tag{25}$$

Here we use the thermophysical property τ to represent the time to stabilize the skin surface temperature.

To fit the model, we take the average temperature at each part to decrease noise.

2.1 Computational Model of Skin

HIFU therapy is a treatment in which ultrasound is applied to the target skin of infected area. During this process, low-level thermal injury occurs to improve microcirculation. The treatment can be considered as a mild burn injury, which will change the physical properties of the target skin area, such as thermal conductance and specific heat capacity [13]. Hence, by quantifying the difference of physical property before and after HIFU treatment, the therapeutic response of HIFU treatment can be accessed.

To ensure the Eq.24 fit our treatment, we used an approximate three-dimensional four-layer skin model to simulate the self-warming process. The values of the parameters defined in each layers in our simulation are represented in table 1.

Table 1. Thermophysical Property Values and Layer Thicknesses in Simulation model. [14].

	d(mm)	C(J kg^{-1} K^{-1})	k(W m^{-1} K^{-1})	ρ(kg m^{-3})	W$_b$(s^{-1})	Q(W m^{-3})
upper dermis	1	3300	0.445	1200	0.00018	368.1
lower dermis	1	3300	0.445	1200	0.00126	368.1
fat	2-5	2674	0.185	1000	0.00008	368.3
muscle	3-6	3800	0.510	1085	0.00270	6684.2

The deepest boundary of the model was set to 37 °C and the original surface 25 °C. We applied a 0 °C cold source on the surface for 60s and removed the cold source to record the self-warming phase, as shown in Figure 1. Eq.24 fitted well to the simulated signal, therefore we used the time thermophysical property τ in Eq.24 in our further study.

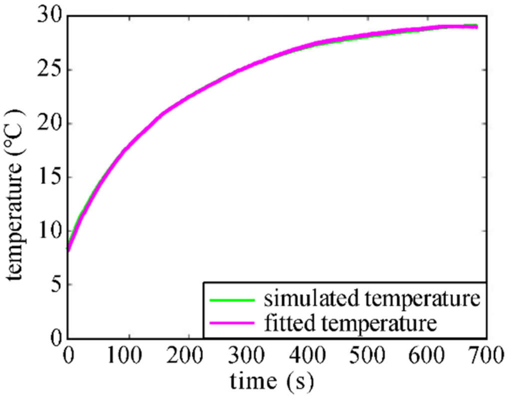
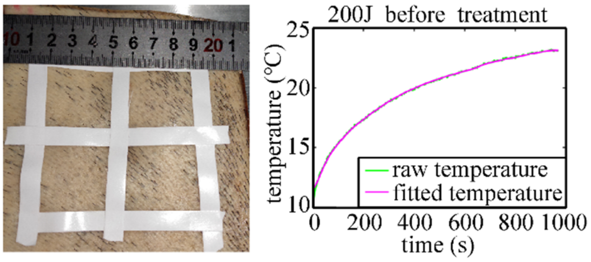


Fig. 1. The simulated temperature curve (green) and the fitted temperature curve (magenta) with Eq.24.

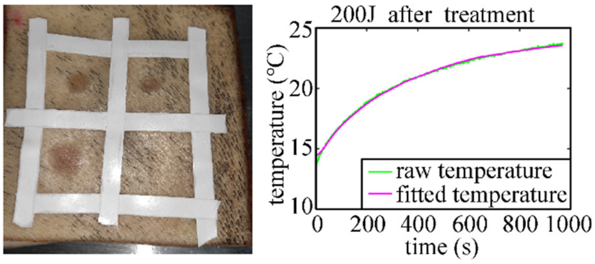
2.2. Pig Skin Statistical Analysis

We used pig skin as the phantom of human skin to explore the relationship between τ and HIFU treatment dose. To reduce individual difference of skin phantom, we applied different HIFU dose on a same pig skin. The HIFU machine used was a Model CZF-300. The transducer's frequency was set to 10 MHz and its power was set to 4 W. Each point was consecutive scanned to attain certain energy. The skin were placed on a constant temperature heating platform (37 °C) to reach stabilization. Ice packs were then applied on affected skin for 60s and removed for self-warming recording. The recording temperature curve and fitting curve from Eq.24 are shown in Figure 2 and Figure 3.



(a) (b)

Fig. 2. Pig skin before HIFU treatment. (a) RGB before treatment. (b) Raw and fitted temperature curve.



(a) (b)

Fig. 3. Pig skin after HIFU treatment. (a) RGB after treatment. (b) Raw and fitted temperature curve.

3 Result and Discussion

The different box plot of τ in each area are shown in Figure 3. The τ before treatment were approximately the same. The τ without treatment (0J control group) remained unchanged after the period of time during the experiment. The τ with different HIFU energy were statistically related to the HIFU treatment dose.

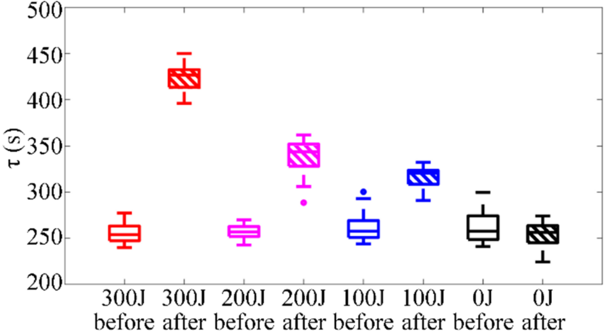


Fig. 4. τ before and after HIFU treatment.

We used the thermal damage rate e to highlight the difference between pre-treatment and post-treatment thermal property change in different parts.

$$e = \frac{\tau_{after} - \tau_{before}}{\tau_{before}} \qquad (26)$$

As shown in Figure 5, the thermal damage rate e was approximate linear correlated to HIFU dose. The thermal damage rate e can be a fast and effective way to quantify the doses in HIFU treatment.

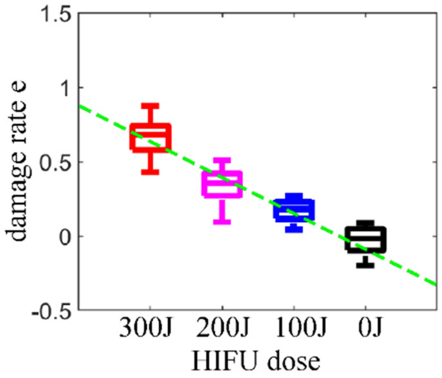


Fig. 5. The relationship between damage rate e and HIFU doses.

4 Conclusion

In this study, we proposed the relevance between thermal damage rate e and local effect of HIFU treatment dose, in order to quickly quantify the effectiveness of HIFU treatment. We will further use this non-invasive method to assess the state of HIFU treatment for VLS as a suggestion for predicting the therapeutic outcome.

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