

ratio of between the required treatment time times for two different cases is equal to a certain constant R exponential to the power of the temperature difference of between the two cases. –The relationship was defined by Dewey *et al.* as:

$$t_1 = t_2 R^{(T_1 - T_2)} \quad (1)$$

where subscripts 1 and 2 represent two different heating situations cases and constant R is can be calculated by:

$$R = e^{-\Delta H / (2T(T+1))} \quad (2)$$

where ~~ΔH~~ ΔH is the enthalpy or inactivation energy of the CHO cells. –In fact, R should not be ~~a~~ considered strictly as a constant, but ~~based on~~ as a temperature-dependent variable. Nevertheless, R was claimed—based on calculations by Dewey *et al.*—to be 0.50 for the CHO cells in the temperature range between of 43 and 46 °C (Dewey, Hopwood 1977, Sapareto and Dewey 1984). For the calculation of R as described by Equation (2), a temperature increment step of 1–°C is adopted. Equations (1) and (2) indicate that if the cell external temperature is to be increased by 1–°C, the therapy acting time required is increased by R times fold.

Nowadays, the internal temperature profile inside of the tissue being heated and several empirical assumptions are have since been incorporated into the thermal dose concept (Arora, Cooley 2005, Damianou, Hynynen 1993, Sapareto and Dewey 1984). This results in the expansion of Equation (1) can be expanded to reflect these assumptions as:

$$t_{ref} = \sum_{t=0}^{t=final} R^{(T_{ref} - \bar{T})} \Delta t, \quad (3)$$

where T_{ref} is the reference internal tissue temperature, typically chosen as 43 °C, t_{ref} is the corresponding therapy time at T_{ref} , and \bar{T} is the average internal tissue temperature during the time interval Δt . Most studies assume $R = 0.50$ is still commonly used, but can be assumed to have different values for can be adopted to reflect different temperature ranges. –The expansion of the thermal dose concept from cell to tissue and from cell external temperature to tissue internal temperature has been widely implemented in ~~the~~ existing studies on thermal therapy (Arora, Cooley 2005, Carstensen, Becroft 1981, Damianou, Hynynen 1993, Frizzell, Linke 1977, Lizzi, Coleman 1984, Overgaard and Suit 1979, Privalov 1996).

Nevertheless, the empirical parameters and experience-based assumptions needed for to predict the expansion may not be unsuitable suitable or accurate for all ranges of temperature. –In this study, the forming formation of a lesion during thermal therapy is interpreted as a denaturation process involving a phase transition. Consequently Under this assumption, part of the input energy is consumed without

註解 [Ed1]:

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註解 [Ed2]:

CHECK: Could you define the “temperature increment step of 1°C” in terms of an equation’s variable? Now, it’s unclear whether 1°C refers to Equation 1’s T_1 or T_2 , or Equation 2’s T .

Also, for Equation 1’s R , do you use Equation 2 to calculate the R using T_1 or T_2 as T ? Consider explaining using the variables T_1 , T_2 , and T , rather than simply ‘temperature’.

~~the~~ an increase of in temperature during the formation of the HIFU ablation lesion (i.e., latent heat of phase transition). In addition, the thermal properties of the tissue change when the lesion forms. The forming of ~~lesion~~ lesions during thermal therapy is therefore not only ~~the resulting~~ a resultant phenomenon arising from ~~exerting~~ a heating action, but also a key factor ~~which can~~ able to influence the history and distribution of the temperature profile. Such an influence ~~is~~ was not considered in the original thermal dose concept and hence has been frequently overlooked in ~~the~~ existing thermal dose models.

The motivation of the present study is to address this significant inadequacy in the original concept of thermal dose. To achieve this goal, the thermal phenomena of ablating pork tenderloins and egg white-based gel phantoms by HIFU are examined in ~~details~~ detail. Theories from classical physics and thermodynamics are adopted to ~~aid~~ the construction of help construct a theoretical model capable of predicting the thermal behaviors of HIFU therapy more accurately. Furthermore, numerical simulations based on the finite element method are performed to explain in detail the

註解 [Ed3]:

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Also, for Equation 1’s R, do you use Equation 2 to calculate the R using T1 or T2 as T? Consider explaining using the variables T1, T2, and T, rather than simply ‘temperature’.