Modeling of Thermal Dose from Focused Ultrasound Exposures for Heterogeneous Tissues

Description of Problem:

The thermal dose calculation is a standard metric in the toolbox of thermal therapies to represent whether a tissue has reached a specific temperature for a sufficient duration in order to cause thermocoagulative necrosis. First described by Saparato and Dewey [1], it is an empirically derived formula that uses an arbitrarily chosen temperature of 43°C for a duration of 240 minutes as the threshold for tissue ablation (240 EM). Thermal dose is calculated cumulatively (as a time integral) and in the case of an MRI-guided intervention on a voxel-by-voxel basis as temperature is measured spatially and temporally throughout treatment.

$$TD(t) = \int_0^t r^{(43-T(t))} dt \qquad \begin{array}{l} r = 0.25 \; (T <= 43°C) \\ r = 0.50 \; (T > 43°C) \end{array}$$

To use this equation in practice, one needs a way to model or measure temperature spatially in tissue and as a function of time in order to map out the region of tissue destroyed by the treatment. In MRI-guided high intensity focused ultrasound (HIFU) it is the MRI, in particular, an MRI sequence and processing algorithm known as proton resonance frequency shift (PRFS) MR thermometry, which provides the temperature information both as a function of space and time. The way the formula works is that for every degree above 43°C the required time to coagulate the tissue halves (120 minutes @ 44°C, 60 minutes @ 45°C, etc.).

This equation is employed in practice without any regard to the type of tissue (organ vs muscle vs bone, etc.) or its surrounding environment (deep seated organ vs superficial). It also does not factor in cooling effects from surrounding heat sinks, such as arterial blood vessels [2]. Qualitatively this algorithm is fairly accurate at predicting the location and extent of the resultant thermal lesion (verified from contrast enhanced MRI imaging and histology) and works well in homogeneous tissues such as bulk muscle or the liver. The two primary concerns with this algorithm within the HIFU community are that it often fails in the presence of noisy temperature data, and that is not as reliable in heterogeneous tissues, such as bone/muscle interfaces or in tissues that are more sensitive to temperature, such as neurovascular bundles. Nerves in particular can ablate at thermal doses well below 240 EM. There is also the overlaying issue that the formula was derived empirically over 30 years ago and there has been little effort into trying to propose a more rigorous model to predict the extent of the thermal lesion created from a HIFU exposure. Dewey revisted the empirical measurements in the mid 90's, and noticed quite a lot of heterogeneity in the thermal dose in various soft tissues [3], but did not test more sensitive tissues such as nerves or more robust tissues such as bone.

Background on Temperature Dependence in Heterogeneous Tissues:

The Pennes Bioheat Equation was derived and validated empirically in human tissues in the late 1940's (back in those days it was OK to perform invasive measurements on your graduate students) [4].

$$\rho c = \frac{\mathrm{d}T}{\mathrm{d}t} = \nabla \cdot k\nabla T - \omega c_b (T - T_b) + Q$$

This partial differential equation takes into account an energy source Q and models the heat transfer in heterogeneous tissues. In this equation ρ is density (kg/m^3), c is specific heat capacity (J/kg/°C), T is temperature (°C), t is time (s), k is thermal conductivity (W/m/°C), ω is blood perfusion (kg/m3/s), Q is heat deposition due to ultrasound (W/m^3), the subscript b refers to blood, and T_b = 37 °C. This model works well in conjunction with the thermal dose model above when the entire heating process is simulated including the simulation of the ultrasonic heating source Q [5]. However, the intraoperative MR thermometry does not provide high spatial resolution like a simulation would, so partial volume effects (averaging of temperature across a size of a voxel when the voxel contains heterogeneous tissues) often underestimate temperature. Recent results from Scott et al. [5] have shown that simulation of temperature and thermal dose from idealized ultrasound sources can produce accurate predictions of the overall ablated volume when targeting heterogeneous tissues such as the spine. However, the prediction of thermal dose directly from a tissue dependant model, when the input parameter is a measured temperature have not been presented in the literature to date.

Problem Challenges:

1. Can a tissue type dependant thermal dose model (similar to the Pennes Bioheat model for tissue heating) be derived that takes into account the thermal conductivity, thermal diffusion, specific heat, and perfusion of the tissue of interest and surrounding structures?
2. Can a spatially dependant (and perhaps a patient specific) thermal dose model be derived which can work directly with intraoperative temperature measurements to better predict the volume of ablated tissue during a MR-HIFU treatment?

References:

[1] Sapareto S.A. and Dewey W.C., Thermal dose determination in cancer therapy. Int J Radiat Oncol Biol Phys, 10(6): p. 787-800 (1984).

[2] Sassaroli E., Li K.C.P., O'Neill B.E., Modeling focused ultrasound exposure for the optimal control of thermal dose distribution. The ScientificWorld Journal, Article ID 252741, 11 pages, 2012.

[3] Dewey W.C., Arrhenius relationships from molecule and cell to the clinic. Int J Hyperthermia, 10: p.457-83 (1994).

[4] Pennes H.H., Analysis of tissue and arterial blood temperatures in the resting human forearm. J Appl Physiol, 1: p. 93-122 (1948).

[5] Scott S.J., Salgaonkar V., Interstitial ultrasound ablation of vertebral and paraspinal tumours: Parametric and patient-specific simulations. Int J Hyperthermia, 30(4): p. 228-244.