Uncertainty Quantification of Thermal Damage in Hyperthermia as a Cancer Therapy

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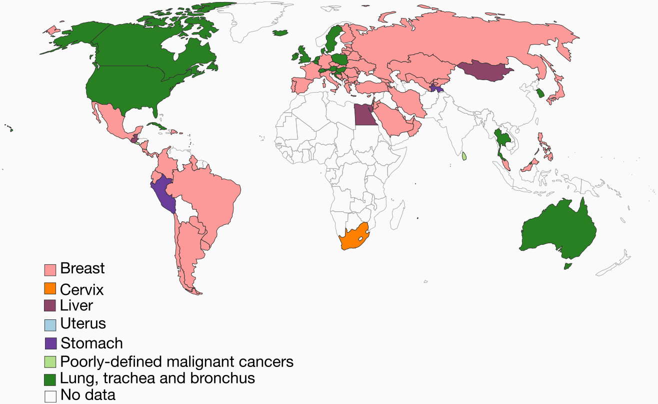
Overview

Introduction

Cancer

Cancer is a major global health issue, and breast cancer is the leading cause of death for the female population in several countries.



Hyperthermia

- Promising non-invasive cancer treatment;
- Overheat the tumour area, inducing necrosis;
- Complement of chemotherapy and radiotherapy treatment;
- One strategy involves using a magnetic nanoparticles ferrofluid.

Matematical Model

Was considered the Pennes equation to simulate bioheat [1]:

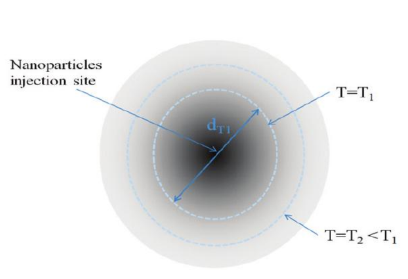
$$
\begin{cases}
\rho c \dfrac{\partial T}{\partial t} = \nabla \cdot k \nabla T + \omega_b \rho_b c_b (T_a - T) + Q_m + Q_r & \text{em } \Omega \times I \\
k \nabla T \cdot \vec{n} = 0 & \text{em } \partial\Omega \times I \\
T(\cdot, 0) = 37,0 & \text{em } \Omega
\end{cases} \tag{1}
$$

[1] Fatigate, G. R., Lobosco, M., and Reis, R. F. (2023). A 3D Approach Using a Control Algorithm to Minimize the Effects on the Healthy Tissue in the Hyperthermia for Cancer Treatment. Entropy, 25(4), 684.

Pennes Model

- Possible to use high energy potential;
- Water-based ferrofluid solution;
- Ferromagnetic fluid with properties 0.1, 0.2 or 0.3 cc;
- SAR [2] is responsible for modeling the overheat generated by the injections.

$$Q_r = \sum_{i=1}^{N_p} A e^{-r_i^2/r_{0,i}^2},$$



[2] Salloum, M., Ma, R., and Zhu, L. (2009). Enhancement in treatment planning for magnetic nanoparticle hyperthermia: optimization of the heat absorption pattern. International Journal of Hyperthermia, 25(4), 309-321.

Pennes Model

Simplifications adopted to the Pennes Model

- The heat transfer occurs by the capillaries;
- Isotropic blood flow;
- The vascular geometry was not considered;
- The temperature of capillaries is equal to the body temperature;

Numerical Scheme

Finite difference method

The solution was approximated using the FDM in a heterogeneous medium using a FTCS

$$
\begin{aligned}
T_{i,j,k}^{n+1} = \frac{h_t}{\rho c}\Bigg[& \frac{k_{i+1/2,j,k}(T_{i+1,j,k}^n - T_{i,j,k}^n) - k_{i-1/2,j,k}(T_{i,j,k}^n - T_{i-1,j,k}^n)}{h^2} + \\
& \frac{k_{i,j+1/2,k}(T_{i,j+1,k}^n - T_{i,j,k}^n) - k_{i,j-1/2,k}(T_{i,j,k}^n - T_{i,j-1,k}^n)}{h^2} + \\
& \frac{k_{i,j,k+1/2}(T_{i,j,k+1}^n - T_{i,j,k}^n) - k_{i,j,k-1/2}(T_{i,j,k}^n - T_{i,j,k-1}^n)}{h^2} + \\
& \rho_b c_b \omega_b \left(T_a - T_{i,j,k}^n\right) + Q_m + Q_r \Bigg] + T_{i,j,k}^n
\end{aligned} \tag{2}
$$

Thermal Damage

Thermal Damage

The thermal damage due to applying the Arrhenius model in the tumor and healthy regions.

$$\Omega(x, y, z, t) = \ln\left(\frac{C(0)}{C(t)}\right) = \int_0^t A e^{\frac{-E_a}{R_u T(x,y,z,\tau)}}\, d\tau. \tag{3}$$

- If the computed damage parameter $\Omega(x, y, z, t)$ reaches 1.0, it is considered that approximately 63.2% of cellular death.
- An Arrhenius damage parameter of 4 suggests that nearly 98.2% cellular death.
- Omega values in the range of $4 \leq \Omega \leq 10$ are considered a complete tumor ablation.

Uncertainty Quantification

Uncertainty Quantification

We applied Monte Carlo with a $1,000$ sample to quantify the uncertainties associated with the two correlated parameters in the Arrhenius model. To analyze the influence of the frequency factor A and the activation energy E_a.

$$E_a \approx 2.63 \times 10^3 ln(A) + 2.46 \times 10^4 \begin{cases} E_{a_u} & = W \sim U(E_{a_{min}}, E_{a_{max}}), \\ A & = e^{3.832 \times 10^{-4} E_a - 10.042}, \end{cases}$$

$$ln(A) = 3.832 \times 10^{-4} E_a - 10.042 \begin{cases} A_u & = W \sim U(A_{min}, A_{max}), \\ E_a & = 2.63 \times 10^3 \ln(A_u) + 2.46 \times 10^4. \end{cases}$$

Results

Execution Ambiance

- C program implementation
- AMD® EPYC$^{\text{TM}}$ 7713
- NVIDIA A100 GPU (for CUDA paralization)
- Single core execution
- Results shown by Paraview
- Execution parameters and domain taken from bibliography

Simulated Scenario

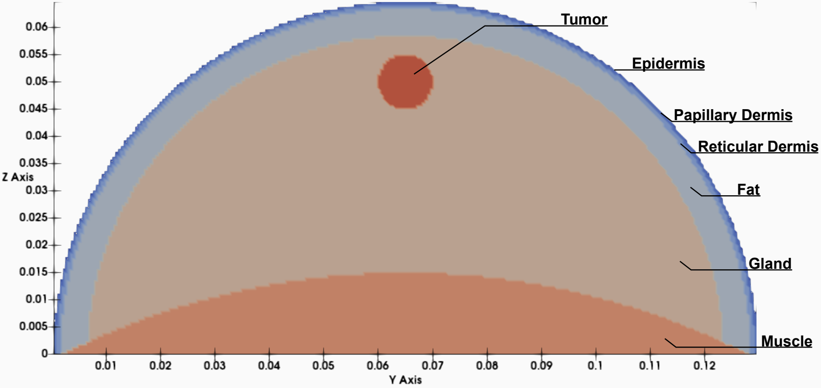


Figure 1: Simulated breast tumor

Heat Spread

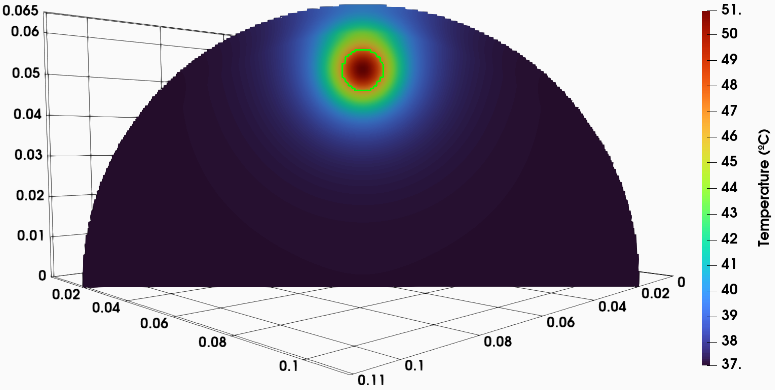


Figure 2: Temperature distribution computed from the bioheat equation at $t = 50\text{min}$

Frequency Factor A Scenario

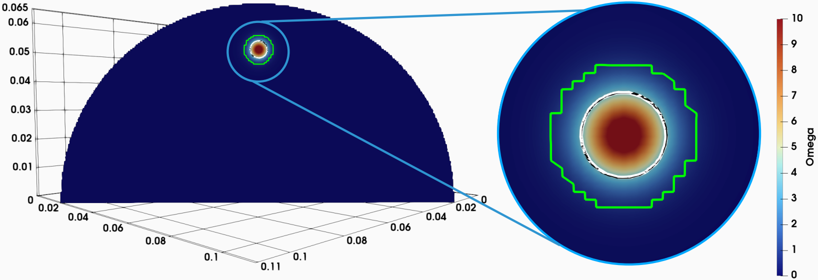


Figure 3: Simulation results for the scenario with uncertainty in the frequency factor A at 5 minutes of treatment.

Frequency Factor A Scenario

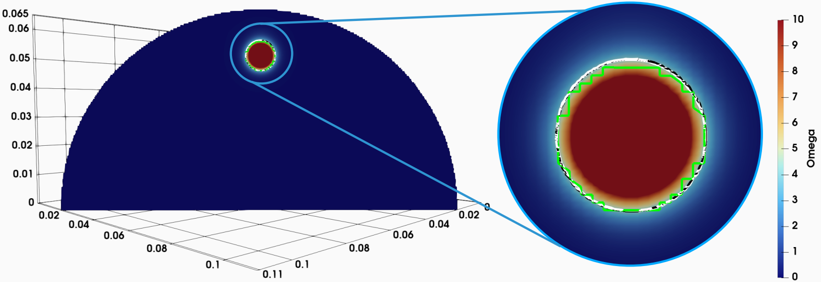


Figure 4: Simulation results for the scenario with uncertainty in the frequency factor A at 10 minutes of treatment.

Frequency Factor A Scenario

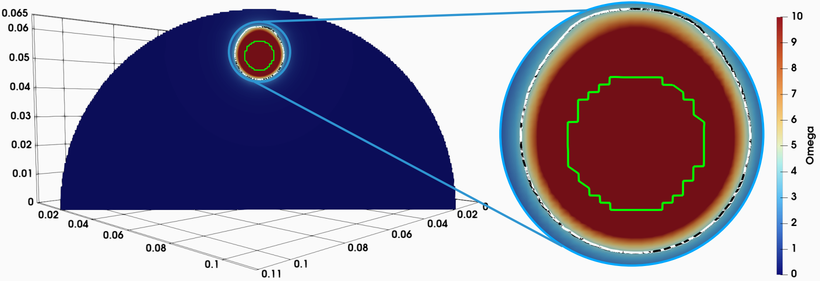


Figure 5: Simulation results for the scenario with uncertainty in the frequency factor A at 50 minutes of treatment.

Frequency Factor E_a Scenario

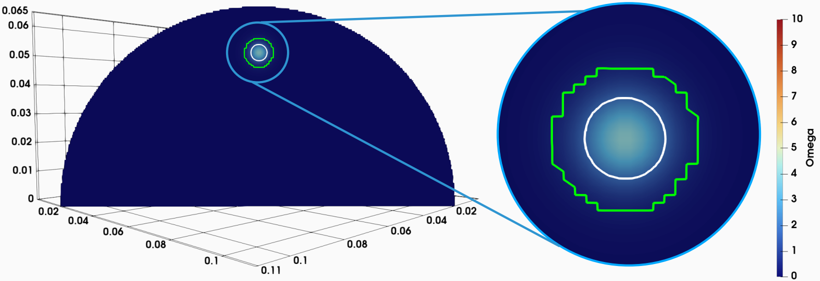


Figure 6: Simulation results for the scenario with uncertainty in the frequency factor E_a at 5 minutes of treatment.

Frequency Factor E_a Scenario

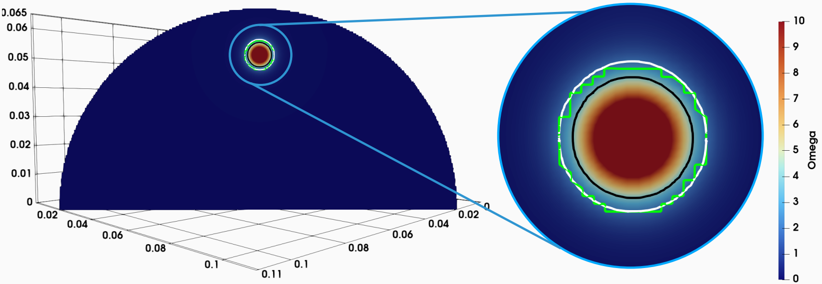


Figure 7: Simulation results for the scenario with uncertainty in the frequency factor E_a at 10 minutes of treatment.

Frequency Factor E_a Scenario

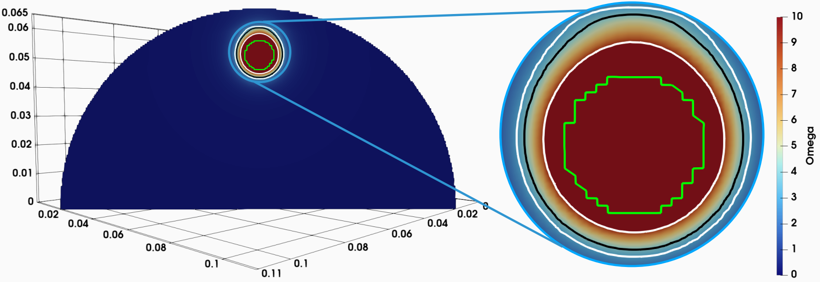


Figure 8: Simulation results for the scenario with uncertainty in the frequency factor E_a at 50 minutes of treatment.

Uncertainty Quantification Results

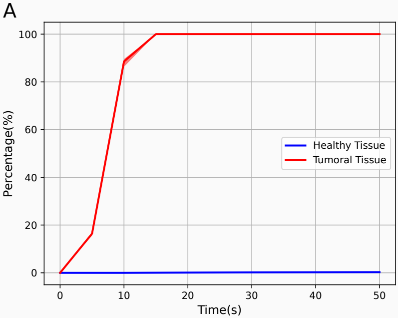


Figure 9: Results of the uncertainty quantification caused by variations in A and E_a for assessing tumor damage during hyperthermia.

Conclusion and Future Works

Conclusion and Future Works

- Variations in the activation energy A have a minor influence on tissue damage predictions.
- However, the variations in the activation energy E_a significantly affect the outcomes.
- The confidence intervals observed in the thermal damage indicate that uncertainty in E_a exists between 15 and 35 minutes to reach the critical damage threshold ($\Omega \geq 4$).

Conclusion and Future Works

- In future works we consider the study of different tissue layers in the human body with realistic tumor and tissue shapes
- Incorporate Multigrid Monte Carlo (MGMC) methods to accelerate simulations and improve computational efficiency
- Finally we intend to validate the model results with clinical or experimental data

Obrigado!

Thanks!

[3] [4]

[3] 423278/2021-5

[4] APQ-01226-21