

Influence of the capillaries bed in hyperthermia for cancer treatment

International Conference on Computational Science 2023
Biomedical and Bioinformatics Challenges for Computer Science

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July 03, 2023

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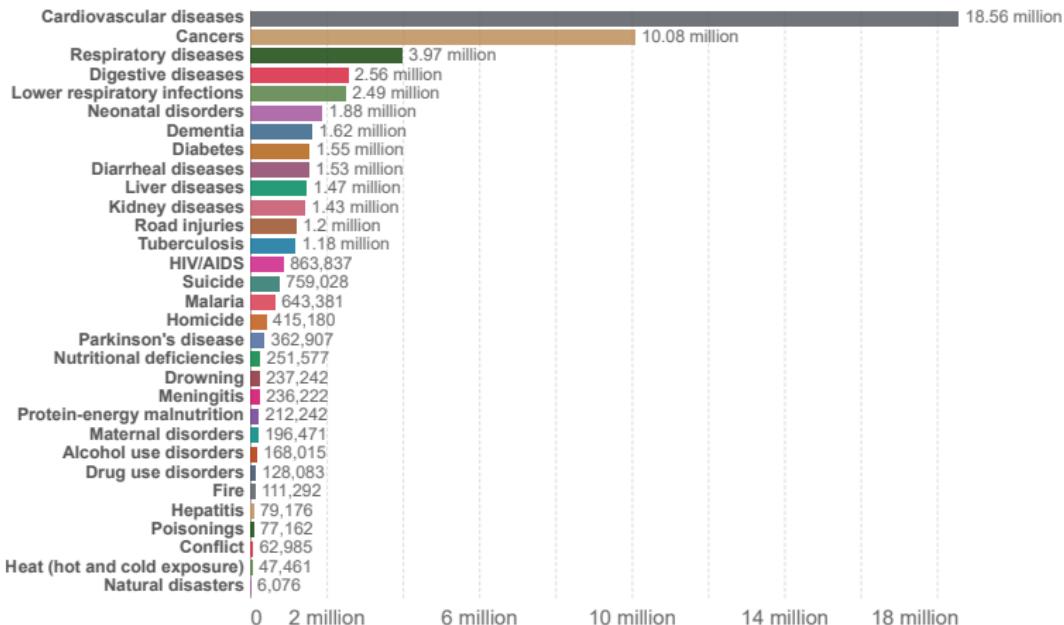
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Motivation

The second biggest cause of death worldwide

Number of deaths by cause, World, 2019

Our
World
in Data



Source: IHME, Global Burden of Disease

OurWorldInData.org/causes-of-death • CC BY

Goals

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- This work presents the computational modeling of solid tumor treatments with hyperthermia using magnetic nanoparticles
- The solution was approximated using the FDM in a heterogeneous porous medium using a FTCS along with an first order upwind numerical scheme
- The Monte Carlo method was employed to quantify the uncertainties of the quantities of interest considered in the simulations
 - a) the influence of the capillaries architecture
 - b) the influence of the blood velocity.

Porous Medium Model

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This study considers the following porous medium model for simulate bioheat ¹

$$\begin{cases} \sigma \frac{\partial T}{\partial t} + \varepsilon (\rho c_p)_b \mathbf{u}_b \cdot \nabla T = \nabla \cdot (\kappa \nabla T) + (1 - \varepsilon) (Q_m + Q_r) & \text{in } \Omega \times I, \\ T(., 0) = 37 & \text{on } \partial\Omega \times I, \\ \kappa \nabla T \cdot \vec{n} = 0 & \text{in } \Omega, \end{cases}$$

where $\sigma = [\rho c_p (1 - \varepsilon) + \rho_b c_{pb} \varepsilon]$, $\kappa = (1 - \epsilon) k_t + \epsilon k_b$.

¹Khaled, A. R., and Vafai, K. (2003). The role of porous media in modeling flow and heat transfer in biological tissues. International Journal of Heat and Mass Transfer, 46(26), 4989-5003.

Heat Source

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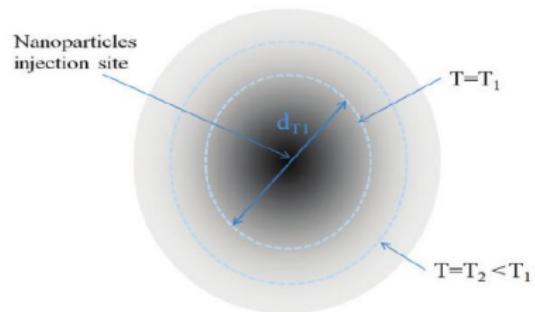
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The specific absorption rate (SAR)² around an injection site is approximated by:

$$Q_r(\vec{x}) = \sum_{i=1}^M A_i e^{-\frac{r_i^2}{r_{0,i}^2}},$$



²Saloum, 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.

Finite Difference Method

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

$$T_{i,j}^{n+1} = \frac{h_t}{\sigma} \left(\varphi_{dif}(T^n) - \varphi_{adv}(T^n) + (1 - \varepsilon)Q_m + Q_r \right) + T_{i,j}^n,$$

where

$$\varphi_{dif}(T^n) = \frac{\kappa_{i+1/2,j}(T_{i+1,j}^n - T_{i,j}^n) - \kappa_{i-1/2,j}(T_{i,j}^n - T_{i-1,j}^n)}{h^2} + \frac{\kappa_{i,j+1/2}(T_{i,j+1}^n - T_{i,j}^n) - \kappa_{i,j-1/2}(T_{i,j}^n - T_{i,j-1,k}^n)}{h^2},$$

Upwind Scheme

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... along with an upwind scheme:

$$\varphi_{adv}(T^n) = \varepsilon(\rho c_p)_b \mathbf{u}_{b_{i,j}} \cdot \begin{cases} \left(\frac{(u_{i,j}^n - u_{i-1,j}^n)}{h} \right) & \text{for } u_{b_x} > 0 \\ \left(\frac{(u_{i+1,j}^n - u_{i,j}^n)}{h} \right) & \text{for } u_{b_x} < 0 \\ \left(\frac{(u_{i,j}^n - u_{i,j-1}^n)}{h} \right) & \text{for } u_{b_y} > 0 \\ \left(\frac{(u_{i,j+1}^n - u_{i,j}^n)}{h} \right) & \text{for } u_{b_y} < 0 \end{cases}$$

where $\mathbf{u}_b = \begin{pmatrix} u_{b_x} \\ u_{b_y} \end{pmatrix}$

Monte Carlo method

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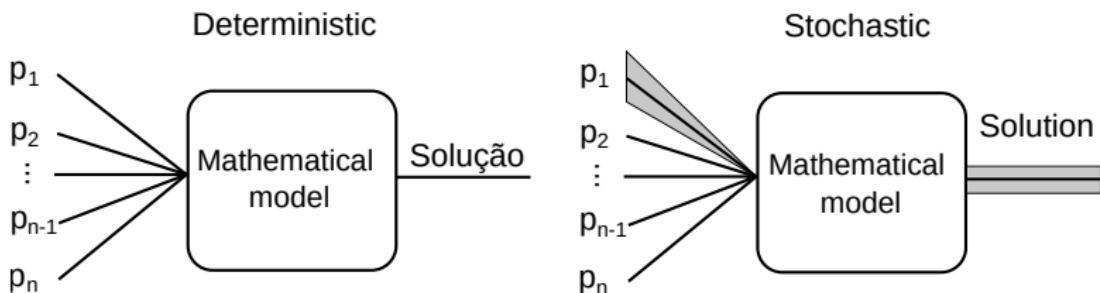
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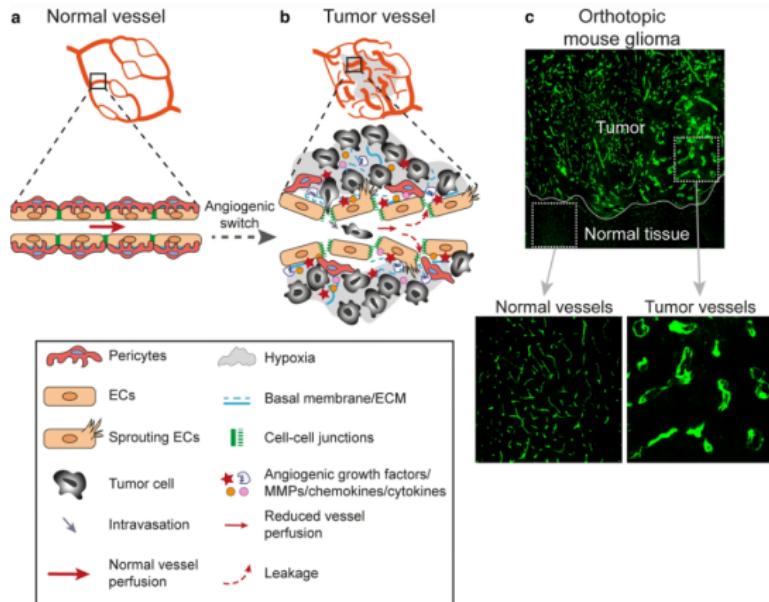
We employ the Monte Carlo method to quantify two uncertainty scenarios:

- the influence of the capillaries architecture
- the influence of the blood velocity



Capillaries Architecture

It is known that tumor growth induces angiogenesis³



³Lugano, R., Ramachandran, M., and Dimberg, A. (2020). Tumor angiogenesis: causes, consequences, challenges and opportunities. *Cellular and Molecular Life Sciences*, 77, 1745-1770.

Capillaries Architecture

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For the capillaries architecture scenario, we analyze the influence of the number of capillaries:

$$N_c = \begin{cases} 70 \times X \sim U(0.7, 1.3) & \text{for the tumor tissue,} \\ 50 \times X \sim U(0.7, 1.3) & \text{otherwise,} \end{cases}$$

and the angle of the capillaries.

$$\theta_c = \theta \times X \sim U(0.7, 1.3).$$

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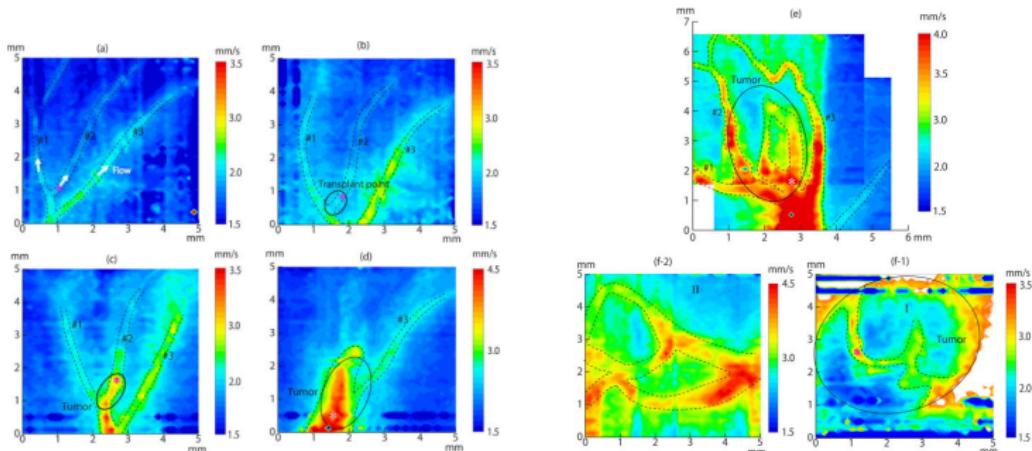
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On the other hand, tumor growth also changes the blood flow ⁴



⁴Ishida, H., Hachiga, T., Andoh, T., and Akiguchi, S. (2012). *In-vivo* visualization of melanoma tumor microvessels and blood flow velocity changes accompanying tumor growth. *Journal of Applied Physics*, 112(10), 104703.

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In the blood velocity scenario, we analyze the influence of the blood velocity:

$$|\mathbf{u}_{\mathbf{b}_c}| = |\mathbf{u}_{\mathbf{b}}| \times X \sim U(0.5, 1.5),$$

Parallel Strategy

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Algorithm 1: Pseudocode of Monte Carlo implementation using OpenMP

```
begin
    # pragma omp parallel
    foreach Monte Carlo Sample do
        foreach  $t_n; n = 0, 1, \dots, N_t$  do
            #pragma omp for
            foreach  $(x_i, y_j); i = 0, 1, \dots, N_x; j = 0, 1, \dots, N_y$ 
                do
                    | evaluate  $T_{ij}^{n+1}$  using Equation (7)
                end foreach
            end foreach
        end foreach
    end
end
```

Simulations Setups

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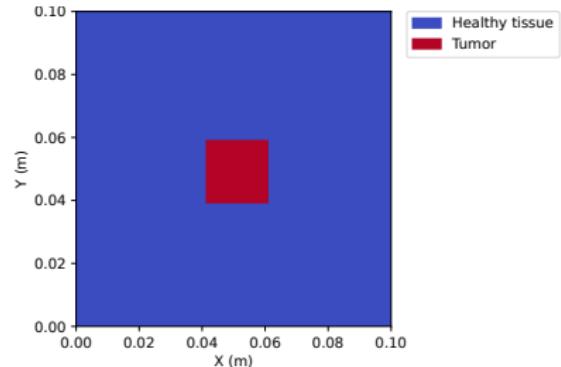
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- We consider squared tumor seated in $(x, y) \in [0.04, 0.06] \times [0.04, 0.06]$.
- For all Monte Carlo simulation we drew 10,000 samples



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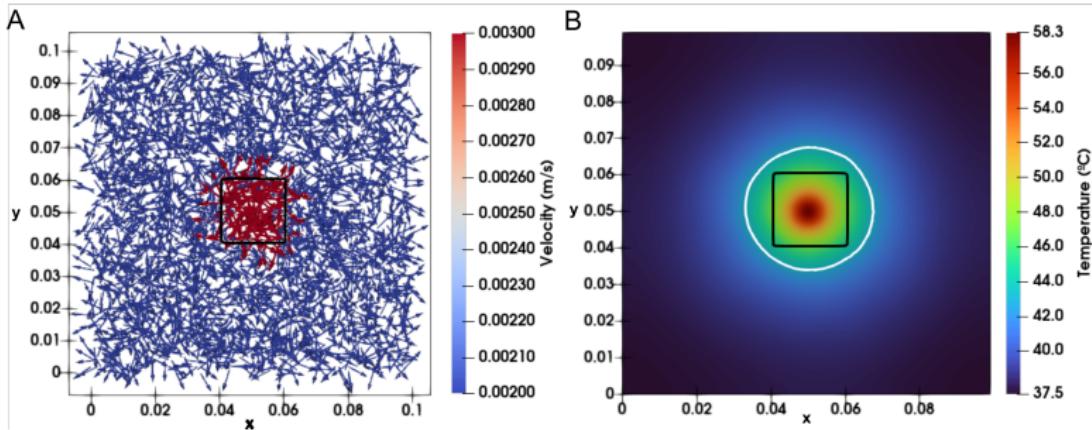


Figure: A) Base velocity field considering tumor tissue with 70% of capillaries terminals and the healthy tissue with 50% of capillaries terminals and **B)** Temperature distribution at $t = 50\text{ min}$

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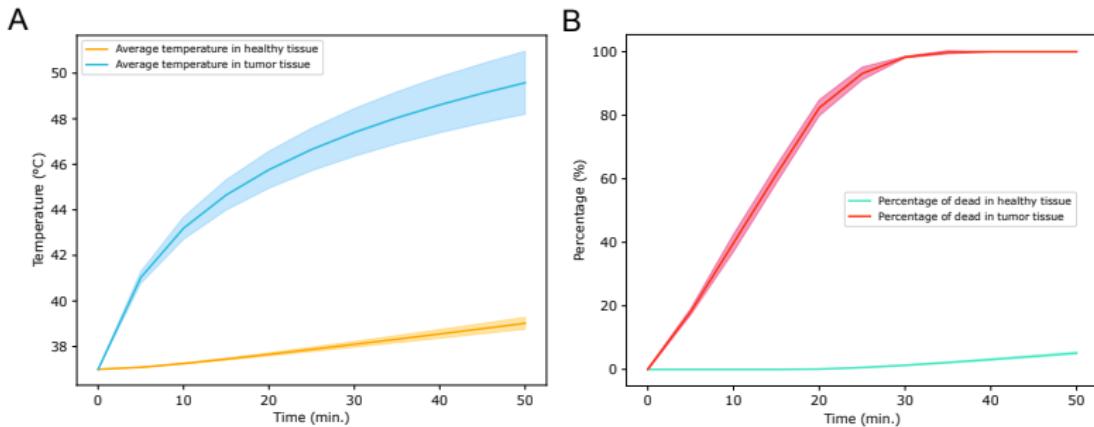


Figure: A) Evolution of temperature and **B)** Percentage of tumor and healthy tissues with $T \geq 43^\circ\text{C}$. Furthermore, only 5.2% of the healthy tissue reached a temperature of 43°C

Angles of capillaries

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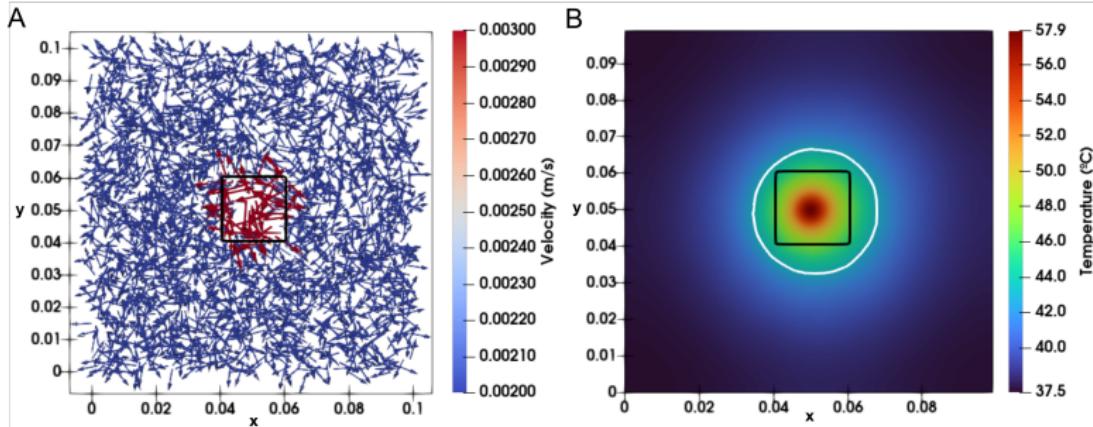


Figure: A) Base velocity field considering tumor tissue with 70% of capillaries terminals and the healthy tissue with 50% of capillaries terminals and **B)** Temperature distribution at $t = 50\text{ min}$

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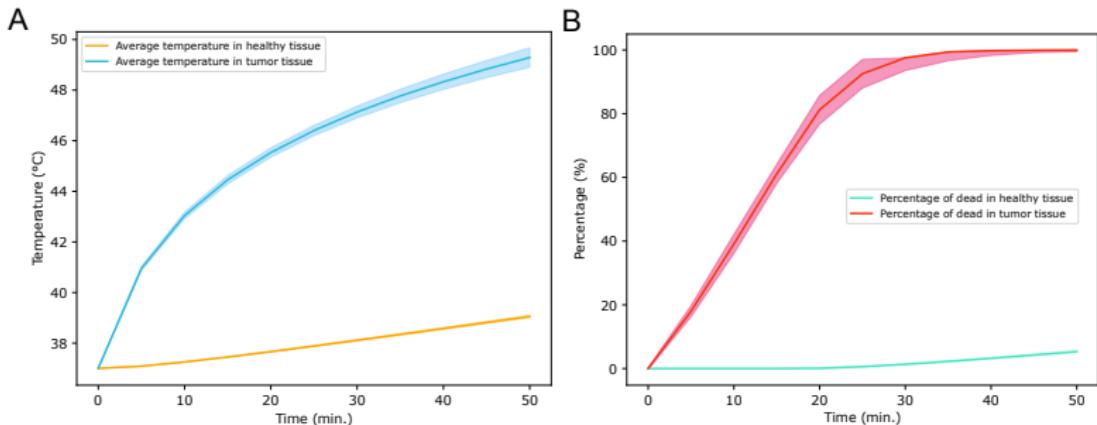


Figure: A) Evolution of temperature and **B)** Percentage of tumor and healthy tissues with $T \geq 43^\circ\text{C}$. Furthermore, only 5.3% of healthy tissue reached a temperature of 43°C or higher

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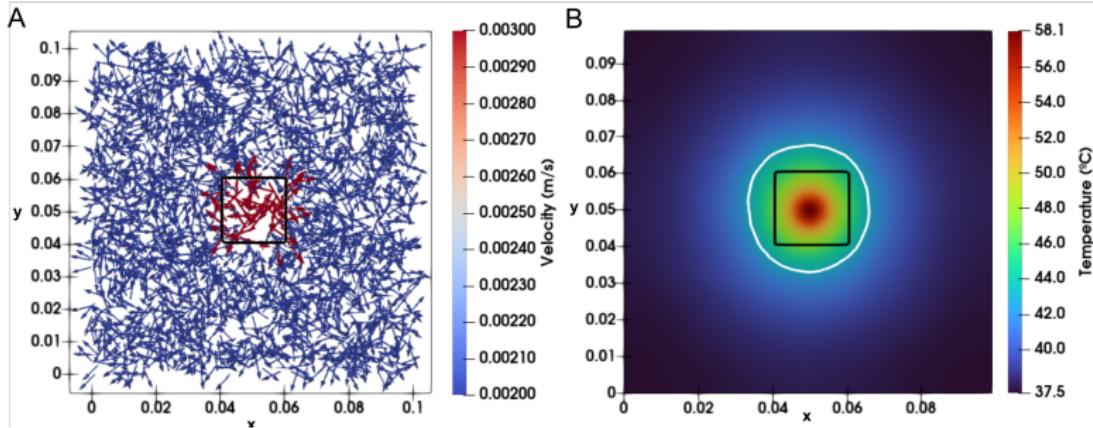


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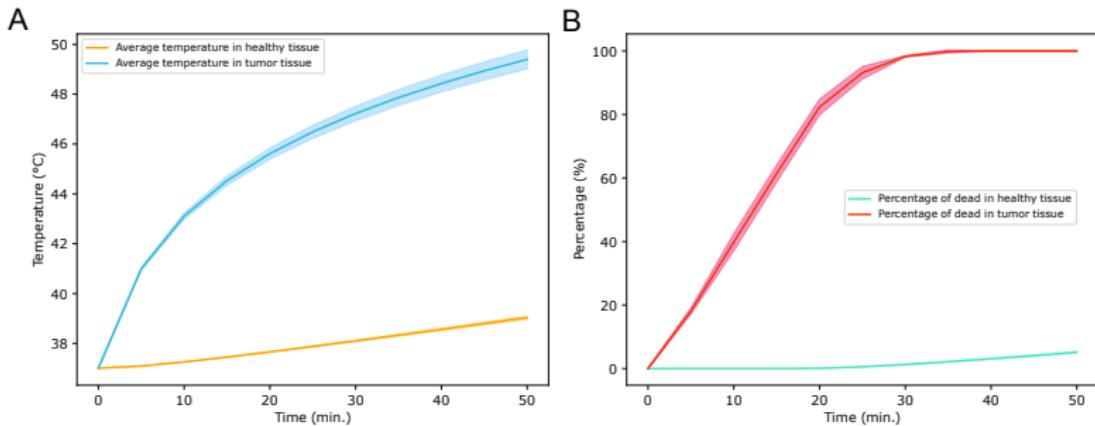


Figure: A) Evolution of temperature and **B)** Percentage of tumor and healthy tissues with $T \geq 43^\circ\text{C}$. Furthermore, only 5.1% of healthy tissue reached a temperature of 43°C or higher

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- The results presented in this study suggest that the capillaries bed architecture significantly influences temperature evolution in the simulated tissue
- Uncertainty analysis can be a powerful tool for treatment planning once it allows the possibility to perform several *in silico* trials and analyze the best option
- The results of this paper reinforce that *in silico* medicine might reduce the need for clinical trials with animals and cohort studies with humans

Future Works

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- Consider the study of different tissue layers in the human body, such as skin, muscle, and fat, along with realistic tumor and tissue shapes
- Determine the uncertain parameters' best probability density function
- Use GPGPU to speedup the implementation.

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Děkuji!
Obrigado!
Thanks!



⁵423278/2021-5

⁶APQ-01226-21

Acknowledgements

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