A Flux-Conservative Finite Difference scheme for the numerical solution of the nonlinear bioheat equation

George C. Bourantas¹, Grand R. Joldes^{1,2}, Adam Wittek¹, Karol Miller^{1,3}

¹*Intelligent Systems for Medicine Laboratory, School of Mechanical and Chemical Engineering, The University of Western Australia, 35 Stirling Highway, Crawley/Perth, WA 6009, Australia*

²*School of Engineering and Information Technology, Murdoch University, 90 South St, Murdoch, Australia*

³*School of Engineering, Cardiff University, The Parade, CF24 3AA Cardiff, United Kingdom*

Abstract

We present a flux-conservative finite difference (FCFD) scheme for solving the nonlinear (bio)heat transfer in living tissue. The proposed scheme deals with steep gradients in the material properties for malignant and healthy tissues. The method applies directly on the raw medical image data without the need for sophisticated image analysis algorithms to define the interface between tumour and healthy tissues.

We extend the classical finite difference (FD) method to cases with high discontinuities in the material properties. We apply meshless kernels, widely used in Smoothed Particle Hydrodynamics (SPH) method, to approximate properties in the off-grid points introduced by the flux conservative differential operators. The meshless kernels can accurately capture the steep gradients and provide accurate approximations. We solve the governing equations by using an explicit solver. The relatively small time-step applied is counterbalanced by the small computation effort required at each time step of the proposed scheme. The FCFD method can accurately compute the numerical solution of the bioheat equation even when noise from the image acquisition is present.

Results highlight the applicability of the method and its ability to solve tumor ablation simulations directly on the raw image data, without the need to define the interface between malignant and healthy tissues (segmentation) or meshing.

Keywords: Flux-Conservative Finite Difference, Tumor Ablation, Bioheat Equation, Meshless Method

Introduction

Image-guided thermal ablation is a minimally invasive treatment of localized solid tumors. Energy sources, like radiofrequency ablation (RFA), microwaves (MW), high-intensity focused ultrasound (HIFU) and light amplification by stimulated emission of radiation (LASER), deliver thermal energy to cancerous lesions. Exposure to heat may render cancer cells more sensitive to radiation or even directly attack cancer cells that show reduced sensitivity to radiation [1,2].

Tumor ablation simulations are based on the Pennes bioheat equation [3]. Herein, we present a flux conservative finite difference method (FCFD) [4 and references therein], which deals efficiently with high discontinuities in the material properties of the tumor and the healthy tissue when solving Pennes equation. During ablation, the material properties are continuously changing and, in some cases, steep gradients occur. The well-established mesh based methods cannot easily deal with sharp interfaces [5], as they work efficiently only for interface conforming meshes. When the mesh does not conform to the interface (cross the interface), mesh based methods fail to provide accurate numerical results for the bioheat equation. Finite difference (FD) methods treat inhomogeneous material properties without any information about the interface. They can be applied directly on a Cartesian grid. Consequently, there is no need for an explicit representation of the interface in the model.

The proposed FCFD scheme can be incorporated into an integrated feedback control system, that integrates computer models with field measurement systems (e.g. Thermal MRI (TMRI), Ultrasound (US)) to allow near-real-time calibration of the models. These integrated systems can provide predictive guidance and control of medical procedures using medical image modalities already available in the operating theatre. Furthermore, the absence of mesh generation drastically decreases the computational burden and provides avenues for a real-time in-situ treatment planning system. The solution method developed in this work employs a flux-conservative finite difference scheme to solve the nonlinear bioheat equations. The scheme uses a Cartesian grid obtained directly from DICOM image data and, therefore, it can be used directly with magnetic resonance thermal imaging. In this paper, we examine the accuracy of the FCFD scheme against a solution method that takes into account the interface between different materials. Furthermore, we show the applicability of the method on realistic image data and examine the computational cost by considering 2D and 3D examples.

The outline of the paper is as follows. In the Methods Section, we present an overview the governing flow equations and discuss the flux-conservative finite difference discretization and the meshless interpolation scheme employed to approximate material properties when computing the heat fluxes. We demonstrate the accuracy and the robustness of the proposed scheme in the Results Section. We summarize the results of using the flux-conservative FD formulation for solving the bioheat equation in the Conclusions Section.

Methods

Governing Equations

The most popular bioheat equation for modeling thermal therapies is the Pennes bioheat equation, which accounts for blood perfusion and metabolic heat generation [3].

$$\rho c \frac{\partial T}{\partial t} = \nabla(k(\mathbf{x}, T) \nabla T) + \omega_b \rho_b c_b (T_a - T) + Q_m + Q_r(\mathbf{x}, t) \quad (1)$$

with ρ (kg/m^3) being the mass density, c [$\text{J}/(\text{kg K})$] the specific heat capacity, k [$\text{W}/(\text{m K})$] the tissue (healthy and malignant) thermal conductivity, and ω_b [$\text{kg}/(\text{m}^3 \text{s})$], ρ_b (kg/m^3), and c_b [$\text{J}/(\text{kg K})$] represent blood perfusion, density, and specific heat of blood, respectively. T_a (K) is the arterial temperature which is treated here as constant, and $T(\mathbf{x}, t)$ is the local tissue temperature. Q_m (W/m^3) is the metabolic heat generation, and $Q_r(\mathbf{x}, t)$ (W/m^3) is the spatial heating rate that is provided by an external heat source. The governing equations represent heat conduction in the tissue, caused by the temperature gradient, and heat transfer between the tissue matrix and local microcirculation.

The majority of bioheat models use the Pennes bioheat equation, which is based on the classical Fourier law and accounts for blood flow through a temperature-dependent heat source term. The Pennes equation cannot capture accurately the effects of large blood vessels. Possible solutions to account for the heat sink caused by large blood vessels would be either to specify an effective convective heat transfer coefficient along the vessel surface or include a complex relationship between blood flow dynamics in the vessel and transient temperature. However, it is widely accepted that even without application of these solutions, the Pennes equation remains a remarkably effective method for modeling heat transfer in tissue during thermal ablation [3].

Pennes equation neglects certain physical phenomena that take place during thermal ablation, mainly water evaporation and thermal tissue damage. Experimental and clinical observations suggest that heating to high temperatures initiates partial evaporation of tissue water [6, 7]. In fact, the entire process of water evaporation, water vapor diffusion, and condensation is a process of water and energy redistribution and is as significant as direct thermal conduction. These processes may become dominant for tissue temperature approaching 100°C . The bioheat equation can be extended to incorporate these phenomena. The power density that is used for evaporation is related to the change in water content of tissue as follows

$$Q_E = -\beta \frac{\partial W}{\partial t} \quad (2)$$

where β is the water latent heat constant, equal to 2260 kJ/kg, and W is the tissue water density (kg/m^3), which is a function of temperature. By using the chain rule, the time derivative of W is

$$\frac{\partial W}{\partial t} = \frac{dW}{dT} \frac{\partial T}{\partial t} \quad (3)$$

Substituting this in Eq. (2) yields

$$Q_E = -\beta \frac{dW}{dT} \frac{\partial T}{\partial t} \quad (4)$$

By including temperature dependent thermal properties and the effect of water evaporation, the extended bioheat equation becomes

$$\begin{aligned} & \left(\rho(T) \frac{dc}{dT} T + \frac{d\rho}{dT} c(T) T + \rho(T) c(T) - \beta \frac{dW}{dT} \right) \frac{\partial T}{\partial t} \\ & = \nabla(k(x, T) \nabla T) + \omega_b \rho_b c_b (T_a - T) + Q_m + Q_r \end{aligned} \quad (5)$$

One of the important challenges in ablation treatment is determining and controlling the amount of tissue damaged during ablation. Several theoretical models have been proposed over the last few years to address this challenge [8]. Measurements have shown that blood perfusion in response to elevated temperature is a complex function of both temperature and time [9, 10]. Moreover, because of differences in the vasculature of tumor, blood perfusion within the tumor is probably quite different from that of normal tissue [11]. Taking these aspects into consideration, tissue thermal damage due to temperature elevations in the tissue over a threshold value for a given time can be described by an Arrhenius-type equation [12]:

$$\Omega = \int_0^t P e^{-\frac{\Delta E}{RT(x,t)}} dt \quad (6)$$

where Ω is a measure of the extent of thermal damage to the tissue, P is a material dependent proportionality constant, ΔE is the material activation energy, and R is the universal gas constant. The undamaged and damaged fractions of the tissue can be written as $f_u = e^{-\Omega}$ and $f_d = 1 - f_u$, respectively. Some of the parameters in the extended bioheat equation can be considered as functions of tissue damage.

Numerical Solution of The Bioheat Equation

Flux-Conservative Finite Difference Scheme

Solving numerically heat conduction in heterogeneous media that include both malignant and healthy tissue is a computationally demanding problem due to the inherent nonlinearity. The identification of different regions and the precise

handling of interfaces require tedious mathematical treatment, mainly for the nonlinear terms and heterogeneities in the material properties, which complicate the solution of the heat conduction problem [13]. The typically used methodology requires the creation of conforming meshes between regions of different conductivity and the calculation of local normal vectors at the tumor/tissue interface, which tends to be a cumbersome for complicated geometries [13].

We propose the flux-conservative finite difference (FCFD) method as a suitable numerical method to solve extended bioheat equation. FCFD method works efficiently on Cartesian grids (that can be directly obtained from DICOM images), and computes the nonlinear convective term $\nabla(k(\mathbf{x}, T)\nabla T)$ by applying a flux-conservative scheme. This scheme computes spatial derivatives for the temperature field using the stencil defined in Fig. 1.

Fig. 1. The stencil configuration used in the flux-conservative finite difference method for (a) 2D and (b) 3D geometry.

This is identical to the classical FD stencil, with the only difference that in the stencils defined in Fig. 1 fluxes in the fictitious grid points $((i+1/2,j)$, $(i-1/2,j)$, $(i,j+1/2)$, $(i,j-1/2)$) are preserved. Flux-conservative finite-difference discretization should be used in cases when the bioheat equation contains a variable thermal conductivity. Computation of the convective term at the grid points $((i,j)$, $(i-1,j)$, $(i,j+1)$, $(i,j-1)$, $(i,j-1)$) will lead to an erroneous non-conservative FD formulation. Application of classical (non-conservative) FD stencil by directly applying the chain rule to compute the spatial derivatives of the convective term will lead to incorrect calculation of thermal fluxes. Therefore, we use flux-conservative FD treatment of bioheat equation, with the nonlinear convection term $\nabla(k\nabla T)$ written as:

$$\nabla(k\nabla T) = \frac{\partial}{\partial x_m} \left(k \frac{\partial T}{\partial x_m} \right) \quad (7)$$

with $m=(x,y,z)$ and using the Einstein summation convention. By using the flux conservative approach, the terms at the central node (i,j) of the stencil shown in Fig.1 can be written (for the x coordinate) as

$$\frac{\partial}{\partial x} \left(k \frac{\partial T}{\partial x} \right) = \frac{k_{(i+1/2,j)} \left(\frac{\partial T}{\partial x} \right)_{(i+1/2,j)} - k_{(i-1/2,j)} \left(\frac{\partial T}{\partial x} \right)_{(i-1/2,j)}}{\Delta x} \quad (8)$$

and, by computing the derivative terms based on the Cartesian grid nodes, can be written as

$$\begin{aligned} \frac{\partial}{\partial x} \left(k \frac{\partial T}{\partial x} \right) &= \frac{k_{(i-1/2,j)}}{(\Delta x)^2} T_{(i-1,j)} - \frac{(k_{(i-1/2,j)} + k_{(i+1/2,j)})}{(\Delta x)^2} T_{(i,j)} \\ &\quad + \frac{k_{(i+1/2,j)}}{(\Delta x)^2} T_{(i+1,j)} \end{aligned} \quad (9)$$

After obtaining the terms for the y - and z - coordinates in the same manner, we can compute the nonlinear convective term in the bioheat equation using Eq. 7. Note that we have to use thermal conductivity values $k_{(i-1/2,j)}$, $k_{(i+1/2,j)}$, $k_{(i,j-1/2)}$ and $k_{(i,j+1/2)}$ for the additional nodes where the heat fluxes are defined. If these values are unknown, they can be computed by e.g. arithmetic averaging of known thermal conductivities on the grid nodes or by using the harmonic average. The former applies for the $k_{(i+1/2,j)}$ conductivity as

$$k_{(i+1/2,j)} = \frac{k_{(i+1,j)} + k_{(i,j)}}{2} \quad (10)$$

while the latter is written as

$$k_{(i+1/2,j)} = \frac{2k_{(i+1,j)}k_{(i,j)}}{k_{(i+1,j)} + k_{(i,j)}} \quad (11)$$

These two approaches, despite their success in delivering reliable results, may result in decreased accuracy of the numerical solution when steep gradients in material properties (higher than 6 orders of magnitude) are present. This is because only the two nodes adjacent to the fictitious point are used in the computation, disregarding all the other nodes in the close vicinity.

Meshless methods are numerical methods initiated two decades ago, which use sophisticated techniques to approximate unknown field functions in point clouds. In the following subsection, we briefly describe the meshless method used to approximate the thermal conductivity at the fictitious points defined in the FCFD stencils.

Meshless Approximation Methods

A number of interpolating/approximating methods are described in the meshless literature [14, 15]. Among them, the most widely used are the Moving Least Squares (MLS) [16], Modified Moving Least Squares (MMLS) [17], Radial Basis Functions (RBF) [15], Discretization Corrected Particle Strength Exchange

(DC PSE) [18] and Smoothed Particle Hydrodynamics (SPH) [14]. Each one of these approximation methods can be used for projecting field values from markers to Eulerian grid nodes. In our approach, we are using SPH kernels, due to their simplicity and low computational cost (there is no need to construct and numerically invert a matrix when computing the shape functions).

In the context of kernel-based interpolation, any function $A(\mathbf{x})$ is approximated by an integral:

$$A(\mathbf{x}) \approx \int A(\mathbf{x}') W(\|\mathbf{x} - \mathbf{x}'\|, h) d\mathbf{x}' \quad (12)$$

where W is the weighting function (or kernel) and h is the smoothing length. Based on the above continuum approximation, a discrete approximation can be obtained as:

$$A(\mathbf{x}) \approx \sum_i A_i W(\|\mathbf{x} - \mathbf{x}_i\|, h) \quad (13)$$

with A_i being the values of the function $A(\mathbf{x})$ at discrete points $\mathbf{x}_i$ and the summation being over particles i located in the support domain of the kernel function. The accuracy of the approximation scheme depends on the choice of the weighting function, which is a normalized function, positively defined, with compact support and monotonically decreasing with increasing distance from the node with coordinate $\mathbf{x}$. Among a variety of possible kernels, we use in our simulations the quadratic kernel

$$W(r, h) = a_Q \left(\frac{3}{16} q^2 - \frac{3}{4} q + \frac{3}{4} \right), \quad 0 \leq q \leq 2 \quad (14)$$

with q being the normalized distance $q=r/h$ and a_Q the dimension-dependent normalization constant.

Results

Code verification

To verify the accuracy of the proposed scheme, the Pennes equation (Eq. (1)) is numerically solved on a rectangular region with dimensions $2L$ ($L=0.05$ m), with a square tumor of size $L/4$ located at the center of the region, as shown in Figure 2a. The physical properties of tissues are realistic, with the thermal conductivity for the healthy tissue given as $k_{HT}=0.5$ W/(m K) and for the tumor $k_T=10$ W/(m K), the density of the tumor and healthy tissue $\rho_{HT}=\rho_T=1052$ kg/m³, heat capacity $c_p=3800$ J/(kg K), blood perfusion for the healthy tissue $\omega_{HT}=0.0001$ s⁻¹ and for the tumor $\omega_{bT}=0.01$ s⁻¹, metabolic $Q_m=4000$ W/m³, and a heating source $Q_r=100$ W/m³ that covers this region. At the boundaries, $h=20$ W/(m² K), $T_f=20^\circ\text{C}$, and $T_a=37^\circ\text{C}$ [12]. The time step is set to $dt=1$ s, and the initial temperature distribution is obtained from the steady state solution [13]. The heating source form used is arbitrarily

chosen; the only purpose is to validate the applicability of the proposed scheme to cases with time-dependent heat sources. The domain has been discretized using 100x50 equally spaced nodes.

Figure 2b presents the transient temperature profiles along the line $x=0$. The results are compared with the ones obtained using the meshless point collocation method [13], which takes into account the boundary between tumor and healthy tissue. The results obtained using the two methods are in excellent agreement.

Fig. 2. (a) Geometry and boundary conditions used in the verification study and (b) transient temperature profiles for the verification test case along the line $y=0$ using the proposed flux-conservative finite difference scheme combined with the meshless approximation method (results are compared against the meshless point collocation method [12], which takes into account the boundary between tumor and healthy tissue)

Example 1: 2D computation of temperature distribution within soft tissue using image data

The next case study considers a random conductivity field with different mean values for the tumor and healthy tissue, similar to the ones obtained from noisy medical images. Using the same problem setup as in the previous example, the conductivity in each region is assigned values that are randomly sampled from a uniform distribution with mean values of $k_{HT}=0.5 \text{ W/(m K)}$ and $k_T=10 \text{ W/(m K)}$ for the healthy tissue and the tumor, respectively, and a variation interval of 10% in both cases. Such data is similar to actual data from medical DICOM images, such as thermal MRI scans, and brings out the frequent, practical problem of a relatively uncertain definition of the precise border between the pathological and healthy parts of the tissue. A gray-scale representation of the conductivity field is shown in Fig. 3a.

We solve the bioheat equation using the flux-conservative finite different solver, without the need to define the interface between the healthy tissue and the tumor. The temperature profile along the midline ($x=0$) is in excellent agreement with that computed in the previous example, which assumes that the conductivity in each region is uniform and equal to the mean value that was prescribed here.

Fig. 3. (a) Gray-scale representation of the random conductivity field with $k_{HT}=0.5$ W/(m K) and $k_T=10$ W/(m K), uniform distributed within a 10% variation interval. **(b)** Transient temperature profiles for the verification test case along the line $x=0$ using the flux-conservative finite difference scheme

Example 2: 3D computation of temperature distribution within soft tissue

We solve the extended bioheat equation in 3D, accounting for water evaporation and tissue damage and considering temperature dependence of all major physical and thermal properties of the tissue (malignant and healthy). Given small changes in density and conductivity, the first two terms in the left-hand side in Eq. (7) can be neglected [19] and the bioheat equation becomes:

$$\left(\rho(T)c(T) - \beta \frac{dW}{dT}\right) \frac{\partial T}{\partial t} = \nabla(k(\mathbf{x}, T) \nabla T) + \omega_b \rho_b c_b (T_a - T) + Q_m + Q_r \quad (15)$$

The dependence of the tissue water content on temperature is obtained by fitting experimental data, to obtain an empirical function [19]:

$$w(T) = \begin{cases} 0.728 + 8.48e^{-2\left(\frac{T-123.286}{16.634}\right)^2} & T \leq 103 \\ 0.024 + \frac{4.531}{1 + e^{\left(\frac{T-30.173}{28.012}\right)^2}} & T > 103 \end{cases} \quad (16)$$

Dynamic changes in blood perfusion rate with temperature and tissue damage are included in the model as

$$\omega_b(T, \Omega) = \omega_{b0} f_T f_u \quad (17)$$

where ω_{b0} is the constitutive perfusion rate and $f_u=1-f_T$, with f_T being a dimensionless function that accounts for vessel dilation at slightly elevated temperatures, which can be approximated as

$$f_T = \begin{cases} 4 + 0.6(T - 42^\circ\text{C}) & 37^\circ\text{C} \leq T < 42^\circ\text{C} \\ 4 & T > 42^\circ\text{C} \end{cases} \quad (18)$$

We solve the extended bioheat equation numerically using the FCFD method over a cubical geometry of length $L=0.02$ m and assuming adiabatic boundary conditions at all six faces. A heat source of finite volume is placed at the middle of a circular tumour of radius 0.002 m.

Fig. 4. Temperature isocontour values ($T=65^\circ\text{C}$) plots at (a) 600 s and (b) 1800 s obtained by using the flux-conservative finite difference scheme. The heat source is placed in the center of the tumor located in the cube center.

The symmetrical geometry setup used facilitates the imposition of thermal boundary conditions. The length of the surrounding tissue has to be large enough compared to the dimensions of the tumor and sufficiently far from the heat source in order for the imposed boundary conditions to accurately describe the actual phenomena. We solve the governing equations for a time of 1800 s, applying a uniform heat source of $Q_r=750 \text{ MW } m^{-3}$. Initially, the temperature is set to $T_0 = 37^\circ\text{C}$ for the entire spatial domain. The material properties are the same as the ones used in reference [19]. Figure 4 shows the isocontour value for $T=65^\circ\text{C}$, obtained using the proposed scheme FCFD method, at different time steps of the ablation treatment.

Conclusions

In the present study, we present a flux-conservative finite difference scheme combined with a meshless approximation method to solve transient bioheat transfer problems using a Eulerian-type approximation. The bioheat equation was extended to account for water evaporation, tissue damage, and temperature-dependent properties. Using this formulation, one can circumvent the need for segmenting the problem domain in order to define the precise interface between healthy tissues and tumor. This simplifies the treatment of parameter discontinuities in the model.

We illustrate the applicability of the proposed method using typical examples that appear in therapeutic treatments, such as ablation of a tumor surrounded by healthy tissues, in two and three dimensions. Comparison of numerical results obtained with other numerical methods, which take into consideration the interface between tissues, showed that the method provides excellent predictions of the temperature profile, both in tumors and in the healthy parts of the tissue, when directly using the image as a model.

Acknowledgements

This research was supported partially by the Australian Government through the Australian Research Council's Discovery Projects funding scheme (project DP160100714). The views expressed herein are those of the authors and are not necessarily those of the Australian Government or Australian Research Council. In addition, we wish to acknowledge the Raine Medical Research Foundation for funding G. R. Joldes through a Raine Priming Grant, and the Department of Health, Western Australia, for funding G. R. Joldes through a Merit Award.

Bibliography

1. van der Zee, J., *Heating the patient: a promising approach?*. Annals of oncology: official journal of the European Society of Medical Oncology/ESMO, 2002. **13**: p. 1173-1184.
2. Moyer, H.R. and Delman, K.A., *The role of hyperthermia in optimizing tumour response to regional therapy*. International journal for hyperthermia, 2008. **24**: p. 251-261.
3. Pennes, H.H., *Analysis of tissue and arterial blood temperatures in the resting human forearm*. Journal of applied physiology, 1948. **1**: p. 93-122.
4. Gerya, T.V., *Introduction to Numerical Geodynamic Modelling*. Cambridge University Press, New York, 2010.

5. Moresi, L., Zhong, S., and Gurnis M., *The accuracy of finite element solutions of Stokes's flow with strongly varying viscosity*. Physics of the Earth and Planetary Interiors, 1996. **97**(1-4): p. 83-94.
6. Yang, D., et al., *Measurement and analysis of tissue temperature during microwave liver ablation*. IEEE Transactions on Biomedical Engineering, 2007. **54**: p. 150-155.
7. Stauffer, P.R., et al., *Phantom and animal tissues for modelling the electrical properties of human liver*. International Journal of Hyperthermia, 2003. **19**: p. 89-101.
8. Dewey, W.C., Diederich, C.J., *Hyperthermia classic commentary: 'Arrhenius relationships from the molecule and cell to the clinic'*. International Journal of Hyperthermia, 2009. **10**: p. 457-483.
9. van Vulpen, M., et al., *Prostate perfusion in patients with locally advanced prostate carcinoma treated with different hyperthermia techniques*. Journal of Urology, 2009, **168**: p. 1597-1602.
10. He, X., et al., *Investigation of the thermal and tissue injury behaviour in microwave thermal therapy using a porcine kidney model*. International Journal of Hyperthermia, 2004. **20**: p. 567-593.
11. Prakash, P., *Theoretical modeling for hepatic microwave ablation*. The Open Biomedical Engineering Journal, 2010. **4**: p. 27-38.
12. Welch, A.J., van Gemert, M., *Optical-thermal Response Of Laser-irradiated Tissue*. Plenum Press: New York, 1995.
13. Bourantas, G.C., et al., *A meshless point collocation treatment of transient bioheat problems*. International Journal for Numerical Methods in Biomedical Engineering, 2014. **30**(5): p. 587-601.
14. Liu, G.R., *Mesh Free Methods: Moving Beyond the Finite Element Method*. CRC Press, 2002.
15. Fasshauer, G., *Meshfree Approximation Methods with MATLAB*. World Scientific Publishers. Singapore, 2007.
16. Lancaster, P., Salkauskas, K., *Surfaces generated by moving least squares methods*. Mathematics of Computation, 1981. **37**(155): p. 141-158.
17. Joldes, G.R., et al., *Modified moving least squares with polynomial bases for scatterd data approximation*. Applied Mathematics and Computation, 2015. **266**: p. 893-902.
18. Bourantas, G.C., et al., *Using DC PSE operator discretization in Eulerian meshless collocation methods improves their robustness in complex geometries*. Computers & Fluids, 2016. **136**: p. 285-300.
19. Bourantas, G.C., et al., *Real-time tumor ablation simulation based on the dynamic mode decomposition method*. Medical Physics, 2014. **41**(5): p. 053301-11.