DEVELOPMENT OF A COMPUTATIONAL PARADIGM FOR LASER TREATMENT OF PROSTATE CANCER

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Collaborators

**ICES**

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http://www.ices.utexas.edu/~feng/dddas/
Goals and Challenges

The Basic Idea

- Living cells in the human body, including cancerous cells, are damaged and destroyed when heated above 44°C
  - when not destroyed, latent defense mechanism activated (HSP)
- Tradeoff: want to damage cancerous tissue but minimize HSP expression
- An interstitial laser can be used to supply energy through optical fibers inserted in the prostate to provide local heating to the tumor
- The locations of fibers and power of the laser can be controlled to eradicate the cancer while minimizing damage to healthy cells and HSP expression in cancerous cells
Goals and Challenges

Laser Based Thermal Therapy over 250 km

Institute for Computational Engineering and Science
U. Texas at Austin

MRTI Facility
M.D. Anderson Cancer Center
Goals and Challenges

The Goals

• To develop mathematical and computational models of laser-induced bio-heat transfer, cell damage, and heat shock protein expression in cancer-infected glands such as the prostate

• To dynamically control laser treatments of cancer through real-time interactions between the computational system and MRTI data of actual treatments of living subjects

• To use these interacting systems to predict and provide unprecedented control over the outcome of laser treatment therapies

Challenges

• Calibration, validation, verification of the computational model

• Remote imaging, parallel adaptive methods

• Real-time control, accurate prediction, minimum damage to healthy tissue, eradication of cancer
Computational Modeling of Bioheat Transfer in Prostate

H.H. Pennes, 1948

D. Yuan, J. Valvano, 2002

M.N. Rylander, et. al., 2005

The Non-Linear Pennes Model

\[ \rho c_p \frac{\partial u}{\partial t} - \nabla \cdot (k(u)\nabla u) + \omega(u)c_{blood}(u - u_a) = Q_{laser}(x, t) \text{ in } \Omega \subset \mathbb{R}^3 \]

\[ -k(u)\nabla u \cdot n = h(u - u_\infty) \text{ on } \partial \Omega \]

\[ u(x, 0) = u^0 \text{ in } \Omega \]

\[ Q_{laser}(x) = 3P \mu_a \frac{\exp(-\mu_s \|x - x_0\|)}{4\pi \|x - x_0\|} \]
The Weak Form of the Pennes Model

Find $u(x, t) \in \mathcal{V} \equiv L^2([0, \tau]; \mathcal{H}^1(\Omega))$ such that

$$B(u, \beta; v) = F(\eta; v) \quad \forall v \in \mathcal{V}$$

$$B(u, \beta; v) = \int_0^\tau \int_\Omega \left[ \rho c_p \frac{\partial u}{\partial t} v + k(u, \beta) \nabla u \cdot \nabla v + \omega(u, \beta)c_{blood}(u - u_a) v \right] dx dt$$

$$+ \int_0^\tau \int_{\partial \Omega} h u v dA dt + \int_\Omega u(x, 0) v(x, 0) dx$$

$$F(\eta; v) = \int_0^\tau \int_\Omega Q_{laser}(\eta; x) v dx dt + \int_0^\tau \int_{\partial \Omega} h u_\infty v dA dt + \int_\Omega u_0 v(x, 0) dx$$
Pennes Model: Thermal Conductivity and Blood Perfusivity
HP finite elements from MRI/MRTI

MRTI Guided Laser Therapy

MRI (Houston)

hp element patch

Co-registration, Segmentation, Mesh Generation (Austin)
The Control Paradigm

Houston (real time)

Initial MRI Data

A

Austin (simulation time)

Initial Mesh Generation/Laser Optimization

B

Pre-treatment

Initial Calibration

Dynamic Control

t=0

Co-registration

Send Real-Time MRTI Data

Calibration

Prediction

i=i+1

Control Loop

Control Step

t=t_i

i=1

1a

\( t=t_i + \Delta t \)

2a

2b

2c

2d

t\_t = t_i + \Delta t

Pre-treatment

Initial Calibration

Dynamic Control
Goal-Oriented Error Estimation

Given a set of model coefficients, $\beta_0$, and laser parameters, $\eta_0$, find the temperature field $u^*(\eta_0, \beta_0)$ such that

$$Q(u(\eta_0, \beta_0)) = \frac{1}{2} \int_0^\tau \int_\Omega (\chi(x)u(x, t))^2 \, dx \, dt$$

satisfies

$$Q(u^*) = \inf_{u \in \mathcal{M}} Q(u)$$

$$\mathcal{M} = \{ u \in \mathcal{V} : B(u, \beta_0; v) = F(\eta_0; v) \quad v \in \mathcal{V} \}$$

where $\chi(x)$ is the characteristic function for region of interest.

$$\delta_u B(u, \beta_0; \hat{u}, p) = \delta Q(u; \hat{u}) \quad \forall \hat{u}$$

$$Q(u) - Q(u^h) = F(\eta_0; p) - B(u, \beta_0; p)$$

$$\delta B(u, \beta_0; \hat{u}, p) \equiv \lim_{\theta \to 0} \frac{1}{\theta} \left[ B(u + \theta \hat{u}, \beta_0; p) - B(u, \beta_0; p) \right]$$

$$\delta Q(u, \hat{u}) \equiv \lim_{\theta \to 0} \frac{1}{\theta} \left[ Q(u + \theta \hat{u}) - Q(u) \right]$$
Calibration of Model

Given a set of laser parameters, $\eta_0$, and an experimentally determined temperature field at time instances $t_n$, within the region $\Omega_\chi \subset \Omega$

$$u_{exp}(x, t_n) \quad x \in \Omega_\chi \quad n = 1, 2, \ldots N_{exp}$$

find the combination of model coefficients, $\beta^* \in \mathbb{P}$, such that

$$Q(u^*(\eta_0, \beta^*), \beta^*) = \inf_{\beta \in \mathbb{P}} Q(u(\eta_0, \beta), \beta)$$

where

$$Q(u(\eta_0, \beta), \beta) = \sum_{n=1}^{N_{exp}} \frac{1}{2} \int_{\Omega} \chi(x) \left( u(x, t_n) - u_{exp}(x, t_n) \right)^2 \, dx \, dt$$

$$+ \frac{\gamma}{2} \int_{\Omega} \nabla \omega_0(x) \cdot \nabla \omega_0(x) \, dx$$

(regularization)

$\chi(x)$ is the characteristic function on $\Omega_\chi$ and the control space $\mathbb{P}$ is defined as

$$\mathbb{P} \equiv \{ \beta \in \mathbb{R}^4 \times C^1(\Omega) \times \mathbb{R}^3 : \exists! \ u \ \text{s.t.} \ B(u, \beta; v) = F(\eta_0, v) \quad \forall v \in \mathcal{V} \}$$
Given a set of model coefficients, $\beta_0$, find the combination of laser power and position, $\eta^* \in \mathcal{P}$, such that

$$Q(u^*(\eta^*, \beta_0), \eta^*) = \inf_{\eta \in \mathcal{P}} Q(u(\eta, \beta_0), \eta)$$

where

$$Q(u(\eta, \beta_0), \eta) = \begin{cases} 
\frac{1}{2} \| u(x, t) - u_{ideal}(x, t) \|^2_{L^2([0, \tau]; L^2(\Omega))} & \text{(Temp. Based)} \\
\frac{1}{2} \| D(u) - D_{ideal}(x) \|^2_{L^2(\Omega)} & \text{(Damage Based)} \\
\frac{1}{2} \| H(u, t) - H_{ideal}(x, t) \|^2_{L^2([0, \tau]; L^2(\Omega))} & \text{(HSP Based)}
\end{cases}$$

and the control space $\mathcal{P}$ is defined as

$$\mathcal{P} = \{ \eta \in C^0([0, \tau]) \times \mathbb{R}^5 : \exists! u \text{ s.t. } B(u, \beta_0; v) = F(\eta; v) \quad v \in \mathcal{V} \}$$
Optimization Framework

Find $q^* \in \mathbb{P}$ s.t.
\[ Q(u(q^*), q^*) = \inf_{q \in \mathbb{P}} Q(u(q), q) \]

where the state variable, $u \in \mathcal{V}$, is determined by a variational PDE of the form
\[ C(u, q; v) = 0 \quad \forall v \in \mathcal{V} \]

$\mathcal{V}$ is the appropriately chosen Hilbert space, and $q$ is a parameter in the control space $\mathbb{P}$

\[ \mathbb{P} \equiv \{ q \in \mathcal{P} : \exists! u \quad \text{s.t.} \quad C(u, q; v) = 0 \quad \forall v \in \mathcal{V} \} \]
Optimization Framework

Given \( q \), find \((u, p)\) s.t.

- **Primal** \( C(u, q; v) = 0 \) \( \forall v \in \mathcal{V} \)
- **Adjoint** \( \delta_u C(u, q; \hat{u}, p) = \delta_u Q(u, q; \hat{u}) \) \( \forall \hat{u} \in \mathcal{V} \)

Compute 1st variation of objective function

- **Control** \( \delta Q(q, \hat{q}) = \delta_q Q(u, q; \hat{q}) - \delta_q C(u, q; \hat{q}, p) \) \( \forall \hat{q} \in \mathcal{P} \)

where

\[
\delta Q(q, \hat{q}) \equiv \lim_{\theta \to 0} \frac{1}{\theta} [Q(u(q + \theta \hat{q}), q + \theta \hat{q}) - Q(u(q), q)] \\
\delta_u Q(u, q; \hat{u}) \equiv \lim_{\theta \to 0} \frac{1}{\theta} [Q(u + \theta \hat{u}, q) - Q(u, q)] \\
\delta_q Q(u, q; \hat{q}) \equiv \lim_{\theta \to 0} \frac{1}{\theta} [Q(u, q + \theta \hat{q}) - Q(u, q)] \\
\delta_u C(u, q; \hat{u}; v) \equiv \lim_{\theta \to 0} \frac{1}{\theta} [C(u + \theta \hat{u}, q; v) - C(u, q; v)] \\
\delta_q C(u, q; \hat{q}; v) \equiv \lim_{\theta \to 0} \frac{1}{\theta} [C(u, q + \theta \hat{q}; v) - C(u, q; v)]
\]
Preliminary Results

- Code Development
  - GMP / Matlab / LBIE for Mesh generation
  - hp3D for parallel data structures and mesh refinement
  - Zoltan for automatic domain decomposition/load balancing
  - PETSc for parallel robust nonlinear equation solvers
  - TAO for optimization
  - GMV/AVS for visualization

- Merging the Infrastructure for Data Transfer and Core Computations

- Profiling and Optimizing
Preliminary Results
Preliminary Results

- 1 gradient computation = 40 linear system solves

- 10 sec simulation (10 gradient computations) w/ 10,000 dof = 8 proc. at TACC running at 10% peak for 5 sec (iterative solver)
Concluding Comments

• Computational infrastructure becoming operational (Aug 2006)

• The possibility of reducing death due to cancer or enhancing the quality of life of patients may represent one of the great triumphs of Finite Element Methods and Computational Engineering

• Nanoshells add further control over the bioheat transfer
ICES Team