DYNAMIC DATA-DRIVEN FINITE ELEMENT MODELS
FOR LASER TREATMENT OF PROSTATE CANCER

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Collaborators

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http://www.ices.utexas.edu/~feng/dddas/
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 images of actual treatments of living subjects.

• To use these interacting systems to predict and control the outcome of laser treatments therapies.

Challenges

• Calibration, validation, verification of the computational model

• Remote imaging, parallel adaptive methods, inverse problems

• Real-time control, accurate prediction, minimum damage to healthy tissue, eradication of cancer
Goals and Challenges

The Basic Idea

- Living cells in the human body, including cancerous cells, are destroyed when heated above 44°C
- A 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

The Models

- High fidelity, valid model of heat transfer
- Cell damage model
- HSP expression model
Laser Based Thermal Therapy over 250 km

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MRTI Facility
M.D. Anderson Cancer Center
Computational Modeling of Bioheat Transfer in Prostate

H.H. Pennes, 1948
S. Weinbaum, L.M. Jiji, 1984
D. Yuan, J. Valvano, 2002
K. Shinohara, 2004
M.N. Rylander, et. al., 2005

The Non-Linear Pennes Model

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

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

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

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

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

\[
B(u, \beta; v) = F(\eta; v) \quad \forall v \in V
\]

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

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

\[
F(\eta; v) = \int_0^\tau \int_\Omega Q_{\text{laser}}(\eta; x) v dx dt + \int_0^\tau \int_{\partial \Omega} h u_\infty v dA dt + \int_\Omega u^0 v(x, 0) dx
\]
Pennes Model: Thermal Conductivity and Blood Perfusivity

![Graphs showing thermal conductivity and blood perfusivity vs temperature.](image-url)
A Family of hp-Finite Element Approximations

\[ u^h = \sum_k \sum_j \alpha_j^k \phi_j(x) \varphi_k(t) \]

\[ \text{span}\{\phi_j\} = \mathcal{V}^{hp} \subset \mathcal{V} \]

\[ B(u^hp; v) = F(v) \quad \forall v \in \mathcal{V}^{hp} \]

Crank Nicolson

\[ \frac{1}{\Delta t} M(\bar{\alpha}^k - \bar{\alpha}^{k-1}) + \bar{g} \left( \frac{\bar{\alpha}^k + \bar{\alpha}^{k-1}}{2}, \bar{\beta} \right) = \bar{f}^{k-\frac{1}{2}} \quad k = 1, \ldots, n \]

\[ \|u - \Pi^{hp}\|_{1,\Omega} \leq C(u) \sum_K \left( \frac{h_K}{p_K} \right)^{\text{min}(p,r-1)} \|u\|_{r,K} \]
HP finite elements from MRI/MRTI

MRTI Guided Laser Therapy

MRI (Houston)

Co-registration, Segmentation, Mesh Generation (Austin)

hp element patch
Theorem Suppose $\Omega$ is Lipschitz. Let $0 < \hat{k}_0 \leq k(u) \leq \hat{k}_1$, $0 < \hat{\omega}_0 \leq \omega(u) \leq \hat{\omega}_1$ and $u^0 \in L^2(\Omega)$. Then

1. There exists a unique solution $u^{hp}(\cdot, t) \in \mathcal{V}^{hp}$ of the semidiscrete Galerkin approximation of the nonlinear Pennes bio-heat transfer model $\forall t \in [0, \tau)$

2. Let $u^{hp} \rightharpoonup u$ weakly in $\mathcal{V}$ for fixed $t$. Then $u$ is a solution of the nonlinear Pennes equation

3. $\forall t \in [0, \tau)$, if $u(\cdot, t) \in \mathcal{H}^r(\Omega) \cap \mathcal{V}$, then

$$\|u - u^{hp}\|_1 \leq C \sum_K \left( \frac{h_K}{p_K} \right)^{\min(p, r-1)} \|u\|_{r,K}$$
Damage and HSP Models (Rylander 2005)

Arrhenius Law

\[ D(u(x, t)) = A \int_0^\tau \exp \left( \frac{-E_a}{R u(x, t)} \right) dt \]

\[ = \ln \left( \frac{\text{initial concentration of healthy cells}}{\text{concentration of healthy cells after thermal insult}} \right) \]

HSP Expression Model

\[ H(u, t) = H_0(u)e^{\alpha(u)t-\beta(u)t^\gamma(u)} \]
The Control Paradigm

Houston (real time)

A

Initial MRI Data

B

Austin (simulation time)

C

Initial Mesh Generation/Laser Optimization

D

Pre-treatment

E

Co-registration

F

Initial Calibration

G

Send Real-Time MRTI Data

H

Prediction

I

Control Step

J

Control Loop

K

Dynamic Control

L

Pre-treatment

M

Initial Calibration

N

Dynamic Control

O

Control Loop

P

t=0

Q

t=t_i

R

t=t_{i+1}

S

t=t_{i+1}
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.

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

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

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

\[
\delta Q(u, \hat{u}) \equiv \lim_{\theta \to 0} \frac{1}{\theta} [Q(u + \theta \hat{u}) - Q(u)]
\]
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

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

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

$\chi(x)$ is the characteristic function on $\Omega_\chi$ and

the control space $\mathbb{P}$ is defined as

$$ \mathbb{P} \equiv \{ \beta \in \mathbb{R}^4 \times C^1(\Omega) \times \mathbb{R}^3 : \exists! \ u \text{ s.t. } B(u, \beta; v) = F(\eta_0, v) \quad \forall v \in \mathcal{V} \} $$
Optimal Control of Laser

Given a set of model coefficients, $\beta_0$, find the combination of laser power and position, $\eta^* \in \mathbb{P}$, such that

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

where

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

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

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

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

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 \( \mathcal{P} \)

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

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

**Primal** $C(u, q; v) = 0 \quad \forall v \in \mathcal{V}$

**Adjoint** $\delta_u C(u, q; \hat{u}, p) = \delta_u Q(u, q; \hat{u}) \quad \forall \hat{u} \in \mathcal{V}$

Compute 1st variation of objective function

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

where

\[
\delta Q(q, \hat{q}) \equiv \lim_{\theta \to 0} \frac{1}{\theta} [Q(u(q + \theta \hat{q}), q + \theta \hat{q}) - Q(u(q), q)]
\]

\[
\delta_u Q(u, q; \hat{u}) \equiv \lim_{\theta \to 0} \frac{1}{\theta} [Q(u + \theta \hat{u}, q) - Q(u, q)]
\]

\[
\delta_q Q(u, q; \hat{q}) \equiv \lim_{\theta \to 0} \frac{1}{\theta} [Q(u, q + \theta \hat{q}) - Q(u, q)]
\]

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

\[
\delta_q C(u, q; \hat{q}; v) \equiv \lim_{\theta \to 0} \frac{1}{\theta} [C(u, q + \theta \hat{q}; v) - C(u, q; v)]
\]
Optimization Framework: Solution Technique

Primal Problems

**Calibration:** Fixed $\eta_0$, at current iterate of $\beta \in \mathbb{P}$
Find $u \in \mathcal{V}$ such that
\[
C(u, \beta; v) \equiv B(u, \beta; v) - F(\eta_0, v) \quad \forall v \in \mathcal{V}
\]

**Optimal Control:** Fixed $\beta_0$, at current iterate of $\eta \in \mathbb{P}$
Find $u \in \mathcal{V}$ such that
\[
C(u, \eta; v) \equiv B(u, \beta_0; v) - F(\eta, v) \quad \forall v \in \mathcal{V}
\]
Optimization Framework: Solution Technique

Adjoint Problems

Calibration:
Fixed $\eta_0$, at current iterate of $\beta \in \mathbb{P}$ and $u \in \mathcal{V}$
Find $p \in \mathcal{V}$ such that

$$\delta_u C(u, \beta; \hat{u}, p) = \delta_u B(u, \beta; \hat{u}, p) = \delta_u Q(u, \beta; \hat{u}) \quad \forall \hat{u} \in \mathcal{V}$$

Optimal Control:
Fixed $\beta_0$, at current iterate of $\eta \in \mathbb{P}$ and $u \in \mathcal{V}$
Find $p \in \mathcal{V}$ such that

$$\delta_u C(u, \eta; \hat{u}, p) = \delta_u B(u, \beta_0; \hat{u}, p) = \delta_u Q(u, \eta; \hat{u}) \quad \forall \hat{u} \in \mathcal{V}$$
Optimization Framework: Solution Technique

Adjoint Problems

Calibration and Optimal Control:

\[ \delta_u B(u, \beta; \hat{u}, p) = \int_0^\tau \int_\Omega \left( -\rho c_p \frac{\partial p}{\partial t} \hat{u} + k(u, \beta) \nabla \hat{u} \cdot \nabla p \right) dx dt + \int_0^\tau \int_\Omega \hat{u} \frac{\partial k}{\partial u} \nabla u \cdot \nabla p + \omega(u, \beta) \hat{u} p \ dx dt + \int_0^\tau \int_\Omega \hat{u} (u - u_a) p \ dx dt + \int_\Omega \hat{u}(x, \tau) p(x, \tau) \ dx + \int_0^\tau \int_{\partial \Omega} h \hat{u} p \ dA dt \]
Optimization Framework: Solution Technique

Adjoint Problems

Calibration:

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

Optimal Control:

$$\delta_u Q(u, \eta; \hat{u}) = \begin{cases} \int_0^T \int_{\Omega} (u(x, t) - u_{ideal}(x, t)) \hat{u} \, dx \, dt \\ \int_{\Omega} \left( \frac{\partial D}{\partial u}(u) - D_{ideal}(x) \right) \hat{u} \, dx \\ \int_0^T \int_{\Omega} \left( \frac{\partial H}{\partial u}(u, t) - H_{ideal}(x, t) \right) \hat{u} \, dx \, dt \end{cases}$$
Optimization Framework: Solution Technique

**Control Problems** Given the state and adjoint variables $u, p \in \mathcal{V}$ compute the first variation (gradient) of the objective function

**Calibration:**

$$\delta_{\beta} C(u, \beta; \hat{\beta}, p) = \delta_{\beta} B(u, \beta; \hat{\beta}, p)$$

$$\delta_{\beta} Q(u, \beta; \hat{\omega}_0) = \gamma \int_{\Omega} \nabla \omega_0(x) \cdot \nabla \hat{\omega}_0(x) \, dx$$

**Optimal Control:**

$$\delta_{\eta} C(u, \eta; \hat{\eta}, p) = -\delta_{\eta} F(\eta; \hat{\eta}, p)$$

$$\delta_{\eta} Q(u, \eta; \hat{\eta}) = 0$$
Target Problem

Red Region: Tumor ($G_T$)

\[ H_{70,27} \leq 1.0 \]
\[ F_D \geq 0.99 \]

Blue Region: Tissue ($G_H$)

\[ H_{70,27} > 1.0 \]
\[ F_D \leq 0.01 \]

Goal here is to optimize laser parameters ($P, \mu_a, \mu_s, x$) based on objective functions defined w.r.t. damage, HSP$_{70,27}$, or temperature.

M.N. Rylander et al., 2005
Insufficient Thermal Dose - $P_1 = 0.5$ W, $P_2 = 0.15$ W
Thermal Overdose - $P_1 = 1.6 \text{ W}, \ P_2 = 1.1 \text{ W}$

Temperature

Cell damage

HSP 70

HSP 27
Damage Based Optimized - $P_1 = 1.0$ W, $P_2 = 0.5$ W

![Temperature](image1)

![Cell damage](image2)

![HSP 70](image3)

![HSP 27](image4)
Multiple Sources

Animation Linux

Animation Windows
Stages of Prostate Cancer

Stage I:
- Ureter
- Lymph node
- Vas deferens
- Bladder
- Seminal vesicle
- Prostate gland
- Rectum
- Urethra
- Cancer

Stage II
Stage III
Stage IV

Cancer may spread to other organs

National Cancer Institute
Cancer Statistics and Standard Treatment Options

- 234,460 new prostate cancer diagnoses in the U.S. in 2006 (33% of all new cancer cases)
- Prostate cancer is a leading cause of cancer deaths in males.
- Prostatectomy usually followed by local radiation therapy
  - major surgery, long recovery time
  - urinary incontinence, urethral stricture, impotence
- 90% of all prostate cancers are discovered in local and regional stages;
- The 5 year survival rates for patients whose tumors are diagnosed at early stages approaches 100%

Quality of Life Post-Treatment an Important Factor

Concluding Comments

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.
ICES Team