Computational Brain Tumor

Integration of models and images for quantitative analysis of tumor growth

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Problem position

• Understanding both the mechanical influence and the diffusion process of gliomas

• Using the model for
  – Identify invaded area that are not visible in the MRI
  – Predict future evolution of the tumor
  – Characterize the tumor
Tumor biology

Necrotic center

Active tumor cells + angiogenesis

Edema and infiltrating tumor cells

Mass effect

T2 MRI

T1 MRI + gad

Tumor cell density

T2 MRI signal

Nécrosis

Observability!
Geometric model

1. Skull.
2. Gray matter
3. White Matter
4. Ventricles
5. Falx cerebri

DTI (atlas)

Initial position of the tumor
Mecanical model

- Linear elasticity for the brain:

\[ \sigma = \lambda tr(\varepsilon) + 2\mu \varepsilon \quad \varepsilon = \frac{1}{2} (\nabla u + \nabla u^T) \]

\( \sigma = \) Stress \quad \lambda, \mu = \text{Lamé Coefficient} \quad \varepsilon = \text{Stress} \quad u = \text{Displacement} 

- Influence of tumor cells on the mechanics

\[ \text{div}(\sigma - \alpha c I_3) + Fe = 0 \]

\( \alpha = \) Coupling factor \quad Fe = \text{External forces} 

Summary:

- Linear relationship force / displacement
- Tumor acts as a local pressure
Diffusion model

Reaction diffusion equation

\[ \frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho c (1 - c) \]

Cell diffusion

Cell multiplication

Flux = 0

Isotropic diffusivity

Anisotropic diffusivity based on the DTI
Tumor Growth simulation
Results

March 2002

March 2002 + initial contour

September 2002

September 2002 + simulation contours
Analyzing Diffusion Model

\[ \frac{\partial c}{\partial t} = \nabla.(D \nabla c) + \rho c(1 - c) \]

- Tumor profile
- Infiltration extent
- Extrapolation
- Not observable from images

- Growth speed
- Parameter Estimation
- Quantification
- Observable from time series of images
Extrapolating Tumor Invasion

- CT and MR have limited resolution for tumor cells.
- We do not see the whole tumor infiltration.
- Use of growth dynamics to understand the extents of the tumor.
Tail Distribution

\[ \frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho c (1 - c) \]

Traveling wave solution in the infinite cylinder with constant D:

\[ c(x, t) = u(x \cdot \hat{n} - vt) = c(\xi) \]

\[ u(\xi) = u_0 \exp \left( -\sqrt{\frac{\rho}{n \cdot (D \hat{n})}} \xi \right) \]

\[ \sqrt{\nabla u \cdot (D \nabla u)} = \frac{1}{\sqrt{\rho u}} \]

\[ t = 63, 90, 125 \text{ days} \]
Comparison with the Model

From 5% to 1% - Using same parameters

After 6 months according to the model

Approximated tails
Invasion Extent vs. Irradiation Margin

Visible tumor

Radiotherapy margin

Simulated probability of finding tumor cells

- Red: Invaded area targeted by radiotherapy
- Yellow: Area targeted by radiotherapy BUT NOT invaded
- Green: Area invaded BUT NOT targeted by radiotherapy
Model Based Growth Quantification

- Observables:
  - Tumor fronts (CTV extent):
    - Tumor infiltrated edema extent for high grade tumors
    - Bulk tumor extent for low grade tumors
  - White matter segmentation and DTI.

- Only $D\rho$ is observable from the images.

- What are growth speeds in the white matter and in the grey matter?
Front Motion Approximation

- Again using the asymptotic traveling wave solution.
- Assuming visible tumor front is an iso-density surface.
- Traveling time formulation for the motion of the tumor front gives:

\[ \sqrt{\nabla T'} D \nabla T = \frac{1}{2\sqrt{\rho}} \]
Identifying Parameters

\[ C(v_w, v_g) = \frac{1}{2} \left[ \text{dist} \left( \Gamma_2, \overline{\Gamma_2} \right), \text{dist} \left( \overline{\Gamma_2}, \Gamma_2 \right) \right] \]

\[ \overline{\Gamma_2} = \begin{cases} x | T(x) = t_2 - t_1, \\ \sqrt{\nabla T' D \nabla T} = \frac{1}{2\sqrt{\rho}}, T(\Gamma_1) = 0 \end{cases} \]

\[ [D\rho]_{wm} = 4.7 \times 10^{-2} \text{ mm}^2 \text{ day} \]

\[ [D\rho]_{gm} = 4.3 \times 10^{-4} \text{ mm}^2 \text{ day} \]
Perspectives I

- Validation of the model through
  - Predicting growth for untreated cases.
- Provide a confidence interval
  - In the extent of the tumor
  - In the tumor cell probability
- Modeling the therapy response
  - Response to drug.
  - Response to irradiation.
- Including more modalities and improving the model.
  - Spectroscopy
  - PET,...
Perspectives II

- Build DTI atlases from healthy subjects
  - Build Non Rigid registration algorithms for DTI
  - Statistical framework in agreement with the application
- Account for mis-registration in the inverse problem formulation
  - Add some local flexibility in the estimation process
- Build real time surgery simulators
- Use the biomechanical model for intra-operative image guided surgery