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Comparative study between spatio-temporal models for brain tumor growth

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ABSTRACT

Modeling of brain tumor growth simulator can estimate life expectancy for individual patients, estimate future effect of brain damages toward human senses and attitude and help in evaluating the efficiency of applied treatments. Brain tumor growth can be calculated based on Spatio-Temporal mathematical models namely the isotropic reaction-diffusion model and the anisotropic reaction-diffusion model where the second model produces more realistic results. Tumor normally grows in White Matter (WM) five times faster than in Gray Matter (GM) which makes brain tissues modeled as inhomogeneous −anisotropic material to assign different parameters to each tissue. In this research a comparative study between several tumor growth models has been achieved to clarify the effect of different algorithms on modeling tumor grow.

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1. Introduction

Cancer is considered one of the leading causes of death worldwide. According to World Health Organization facts sheet that was published on February 2017 where it causes about 13% of all deaths [1,2]. Tumor can be defined as an abnormal mass of tissue which is resulting from an abnormal growth or division of cells [3]. The most common methods for diagnosing of tumors are Magnetic Resonance Imaging (MRI) and CT-Scans. According to statistics, metastatic tumors are more occurrence than primary tumors [4] and incidence of malignant tumors ratio is more than benign tumors [5]. The most common primary central nervous system tumor that forms more like 80% of all malignant brain tumors is Glioma [6]. Glioma can be classified according to the tumor growth rate into High-Grade Glioma (HGG) or Low-Grade Glioma (LGG). The HGG is the most common type of primary brain tumor. Standard treatments for HGG are surgery, radiation therapy and chemotherapy [5,7]. There are many mathematical models which simulate tumor growth. They are either cellular models or whole tissue models [8]. Cellular models such as Cellular Automata (CA) model [9–12] describe the cellular division depending on some probability methods (game of life). However, whole tissue models rely on Reaction Diffusion Equation (RDE) [8,13–28]. RDE models are more realistic in results because they depend on real data of the brain tissues' structure. Modeling of brain tumor growth simulator can estimate life expectancy for individual patients, estimate future effect of brain damages toward human senses and attitude and help in evaluating the efficiency of applied treatments.

This study presents survey of different brain tumor growth models which are using RDE and comparative study between their results for Glioma modeling. This study does not take into consideration treatment therapies modeling, but it focuses on behavior of tumor growth using different parameters and models.

2. Materials and methods

2.1. DTI dataset

Diffusion tensor imaging (DTI) is a magnetic resonance imaging technique that enables the measurement of the restricted diffusion of water in tissue [29–34]. In three-dimensional space, the generalized diffusion tensor is a symmetric, positive definite, second-order 3×3 matrix D. Because D is symmetric and positive definite, its three eigenvectors (principal coordinate directions) $\boldsymbol{e}_1$, $\boldsymbol{e}_2$ and $\boldsymbol{e}_3$ are orthogonal. The corresponding eigenvalues (diffusion coefficients) for these vectors are λ_1, λ_2 and λ_3 respectively such that $\lambda_1 > \lambda_2 \cong \lambda_3$. The first eigenvector $\boldsymbol{e}_1$ gives the main diffusion direction, which corresponds to the fiber direction, and the other two eigenvectors are in the cross-fiber direction.

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$$D = E\Lambda E^T = [\boldsymbol{e}_1 | \boldsymbol{e}_2 | \boldsymbol{e}_3] \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} \begin{bmatrix} \boldsymbol{e}_1 \\ \boldsymbol{e}_2 \\ \boldsymbol{e}_3 \end{bmatrix} \quad (1)$$

DTI images can be described using rotational invariant quantities such as Mean Diffusivity (MD) and Fractional Anisotropy (FA), Rational Anisotropy (RA), the Linear Anisotropy (C_l), Planner Anisotropy (C_p) and Spherical Anisotropy (C_s) indices [32–34].

Datasets used in this work are acquired from Laboratory of Brain Anatomical MRI of John Hopkins Medical Institute website. These datasets consists of volumes of brains DTI data. Each brain DTI volume contains 50 slices of 256×256 voxels per slice. Each dataset has a file consists of 35 gradient orientations used to calculate tensor data. In every slice, voxel width = 0.9375 mm, voxel height = 0.9375 mm and space between two successive slices = 2.5 mm.

2.2. Spatio-Temporal models of tumor grow

Spatio-Temporal models of tumor growth have been widely used in the literature for modeling the growth of brain Glioma [8,13–28]. These models describe the evolution of the pathology via proliferation time of tumor cells and infiltration space into the surrounding tissue based on Reaction–Diffusion Equation (RDE). The simplest RDE can be derived based on 2nd Fick's law, and Kolmogorov-Petrovsky-Piskounov (equation (1)). The isotropic version of the equation is represented by equation (2)

$$\frac{dc}{dt} = \nabla \cdot (D(x) \nabla c) + R(c) \quad \text{Anisotropic} \quad (2)$$

$$\frac{dc}{dt} = D(x) \nabla^2 c + R(c) \quad \text{Isotropic} \quad (3)$$

where $D(x)$ is the spatially resolved diffusion tensor that describes cell diffusion rate at certain point x in time t, c is the Glioma cell concentration of the same point x and at the same time t. The function $R(c)$ represents the proliferation component where it is the temporal evolution pattern of the growth. Some researches [8,13,18,20,21] tends to include treatment therapy function $T(c)$ to the equation which makes equation (6) takes the form:

$$\frac{dc}{dt} = \nabla \cdot (D(x) \nabla c) + R(c) - T(c) \quad (4)$$

The diffusion tensor $D(x)$ has been represented in the literature with different forms and parameters values. The general form can be represented by the following equation:

$$D(x) = D_{WGC}(x) W(x) \quad (5)$$

where $D_{WGC}(x)$ is the inhomogeneous diffusion coefficient, and $W(x)$ is the diffusion tensor. Inhomogeneous diffusion coefficient $D_{WGC}(x)$ can be determined using:

$$D_{WGC}(x) = \begin{cases} D_{WM} & if \quad x \in WM \\ D_{GM} & if \quad x \in GM \\ D_{CSF} & if \quad x \in CFS \end{cases} \quad (6)$$

Such that, D_{WM}, D_{GM} and D_{CSF} are diffusion coefficients for White Matter (WM), Gray Matter (GM) and Cerebrospinal fluid (CSF) respectively. Different values have been assigned to these for both High Grade Glioma (HGG) and Low Grade Glioma (LGG); however, the most preferred values in normalized scale are 1, 0.2 and 0 for D_{WM}, D_{GM} and D_{CSF} respectively where this will keep five-fold difference between the WM and the GM. The weighted diffusion tensor $W(x)$ has represented using different models such as:

Model 1 (M1) [16,17,27]:

$$W(x) = I = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}. \quad (7)$$

Model 2 (M2) [18,22]:

$$W(x) = \begin{cases} \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} & x \ \varepsilon \ WM \\ I & x \ \varepsilon \ GM \end{cases} \quad (8)$$

Model 3 (M3) [25]

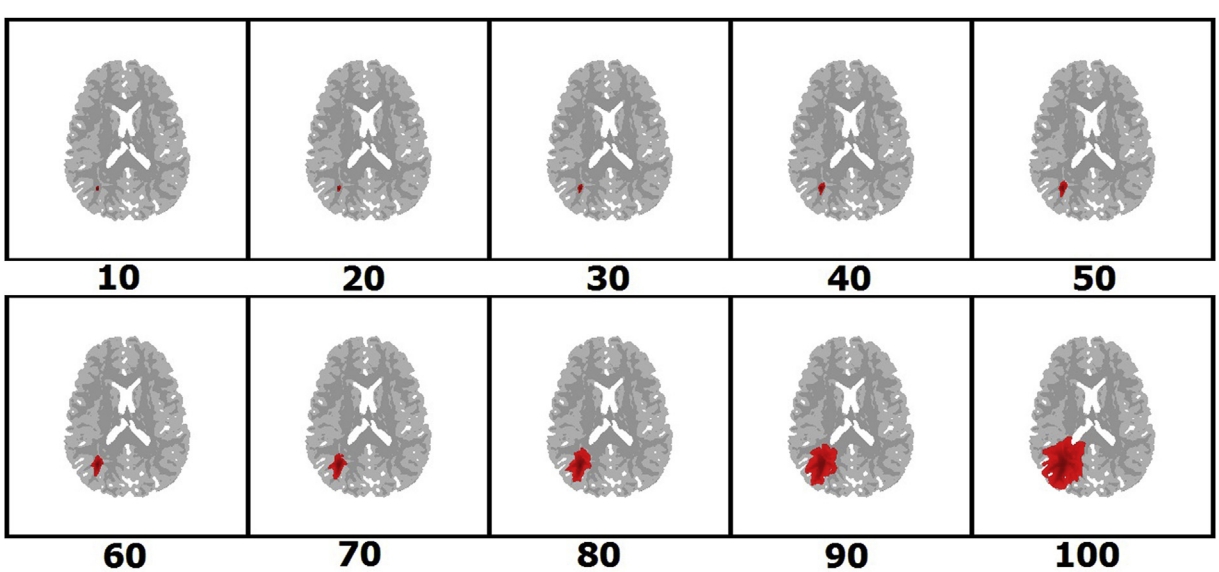

Fig. 1. Sample simulation of primary Glioma growth.

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