Implementation of Finite Difference Method for Detecting Brain Tumor Growth

by

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LIST OF ABBREVIATIONS

1D	One dimensional
2D	Two dimensional
3D	Three dimensional
CN	Crank-Nicolson
CT	Computerized tomography
FDM	Finite difference method
GBM	Glioblastoma multiforme
PDEs	Partial differential equations

LIST OF SYMBOLS

D	Diffusion coefficient
D_g	Constant for x in gray matter
D_w	Constant for x in white matter
Δt	Time step size
Δx	Spatial step size
∇	Spatial gradient
ρ	Growth rate

Pelaksanaan Kaedah Perbezaan Terhingga Untuk Mengesan Pertumbuhan Tumor Otak

ABSTRAK

Pertumbuhan tumor otak adalah salah satu kanser yang berbahaya di dunia yang menyebabkan kematian. Dalam usaha untuk membantu orang ramai untuk menyedari tentang tumor otak, pengesanan pertumbuhan tumor telah dilakukan. Ia juga boleh mencegah penyakit menjadi teruk. Glioma adalah tumor otak primer yang paling umum. Ia adalah satu kumpulan tumor otak primer yang berbeza dan mempunyai keupayaan menembusi seluruh otak. Persamaan reaksi resapan berdimensi satu telah digunakan untuk mengesan pertumbuhan tumor otak. Untuk menyelesaikan persamaan reaksi resapan, proses pendiskretan telah dilakukan dengan menggunakan kaedah tersurat.. Satu persamaan resapan telah digunakan untuk mengesahkan kaedah-kaedah ini. Selepas proses pengesahan, algoritma-algoritma berangka telah dibangunkan dalam perisian MATLAB untuk menyelesaikan persamaan reaksi resapan berdimensi satu untuk pertumbuhan tumor otak. Untuk tujuan simulasi, syarat-syarat sempadan dan syarat awal, langkah-langkah ruang dan langkah masa telah ditentukan. Masalah ini telah diselesaikan dengan mengguna kaedah tersurat untuk dua masalah berbeza. Penghampiran perbezaan terhingga menggunakan tersurat telah dibentangkan secara grafik. Keputusan simulasi bagi persamaan reaksi resapan berdimensi satu berjaya mengesan kelakuan pertumbuhan tumor otak yang mengambil kira jirim kelabu dan jirim putih.

Implementation of Finite Difference Method for Detecting Brain Tumor Growth

ABSTRACT

Brain tumor growth is one of the dangerous cancers in the world that cause death. In order to help people to be aware about brain tumor, detection of tumor growth has been done. It can also prevent the disease to become worst. Gliomas are the most common primary brain tumor. It is a disparate group of primary brain tumor and has the ability of penetrating diffusely throughout the brain. One dimensional reaction diffusion equation has been used to detect the brain tumor growth. The simulation of numerical modeling was conducted to detect the tumor growth. In order to solve reaction diffusion equation, the discretization processes have been done using explicit methods. A diffusion equation is used to validate these methods. After validation process, numerical algorithms are developed in MATLAB software to solve one dimensional reaction diffusion equation for brain tumor growth. For the purpose of the simulation, the boundary condition and initial conditions, the spatial steps and time steps are determined. This problem has been solved using explicit method for two difference problems. The finite difference approximations using explicit methods are presented graphically. The simulation results of one dimensional reaction diffusion equation successfully detect the behaviour of the brain tumor growth which considered the grey and white matter.

CHAPTER 1

INTRODUCTION

1.1 Overview

The human body is made up of various kinds of cells. Every type of the cells has special roles. The cells distribute in an orderly way as they grow in the body to produce new cells so they can keep the body healthy and working properly. When they lose the ability to manage the growth, the cells will divide frequently with none order. Tumors were named after extra cells from a mass of tissue. A brain tumor is a growth of the abnormal or normal cells in a right place in the brain. A primary brain tumor is one which begin inside the brain. Non-cancerous (benign) and cancerous (malignant) were a grouped of primary tumors(Berger & Wilson, 1999).

Benign brain tumors commonly grow slowly. Based on their specific area inside the brain, it can be removed by surgery. Malignant brain tumors are usually named brain cancer which tends to grow quickly dispersal around brain tissue and regularly cannot be totally detached surgically. Since there is no identified purpose of brain tumors, there are no method to stop them (De Angelis, 2001). Brain tumors or gliomas are amongst the toughest forms of cancer to treat since the brain of human is such a significant and difficult organ (Swan & Murtha, 2015). Thus, while killing the cancer cells, special cares must be considered by the doctors so that brain tissue is not damage.

Infiltrating the brain far beyond the visible tumor mass was a very challenging chore since the brain cancer cells were very diffuse. It means, if brain tumor wants to be treated effectively, the treatment not only what we can see, but also what we cannot see.

Parabolic equation has been used in many applications like brain tumor and breast tumor growth (Pheng, Norma & NorFarizan, 2007; Islam, Norma & Ping,2011). For the simulation of brain tumor growth using parabolic equations, it desires us to see the definition of partial differential equations (PDEs) (Moseyabi, 2010). Physically, parabolic PDEs have a tendency to rise in time dependent diffusion problems, for example the transient flow of heat in accordance with Fourier's law of heat conduction.

In sciences, mathematical model often used to predict or describe observation in the real world. For more understanding and gain valuable perceptions into different parts of solid tumor growth, mathematical modelling acts as an important role in assisting biomedical researchers. Murray (2003) stated that mathematical modelling of biomedical phenomena can be very useful in analysing issues that can donate to the complexity intrinsic in insufficiently understood developmental process disease. Mathematical models have been developed to quantify the proliferation and invasion dynamics of glioma within anatomically accurate heterogeneous brain tissues based on the current knowledge of the properties of gliomas.

In this research, an explicit finite difference method will be used to solve the one dimensional (1D) reaction diffusion equation for detection of brain tumor growth.

1.2 Problem Statement

Brain tumor are the most dramatic form of human illness and among the most rapidly fatal of all cancers. Only about half of the patients with brain tumors are still alive one year after diagnosis. Statistic in Sarawak from January 2009 until December 2012 showed that, the incidence of brain tumors is 4.6 per 100,000 population/year, higher than the national statistics which estimated by Globacon 2012, saying Malaysia brain tumors and other nervous system age standardised incidence to be 2.8 per 100,000 population / year with cumulative rate 0.3%, Meningioma is the common brain tumor, accounting for 32.3%. Based on the fact stated earlier, this study will be conducted in order to detect the growth of brain tumor and prevent the disease becomes worst. In this study, 1D reaction diffusion equation will be used in order to detect the growth of brain tumor using finite difference method. Later, by applying the finite difference method, the simulation of brain tumor growth will be implemented and the growth of tumor cell can be described.

1.3 Objectives

The main objective of this study is to detect the brain tumor growth. In order to achieve the main objective, the following sub-objectives will be carried out:

(a) To discretize 1D reaction diffusion equation using explicit finite difference methods.

(b) To develop numerical algorithms and procedures for solving 1D reaction diffusion equation.

(c) To verify the accuracy of the selected finite difference method in predicting the growth of brain tumor

1.4 Scope of Study

In this study, the work is focused on solving the 1D reaction diffusion equation for brain tumor growth. Explicit method is selected to solve this equation. The brain tissues which are grey and white matters are also considered in this study in order to detect the growth of tumor. The simulation for detecting brain tumor growth will be implemented in MATLAB to provide the approximate solutions of tumor growth.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

This chapter will review the existing researches on the mathematical modeling in solving the brain tumor growth problem. First, the discussion will be on the brain tumor growth, and followed by gliomas which will be elaborated and discussed. Finally, the discussion will be on the numerical methods for solving the reaction diffusion equation.

2.2 Brain Tumor Growth

A brain tumor is one of the prevalent cancers in the world and one of the main causes of death from cancer. It was a powerful system in which bad cells grow and spread, ultimately overpowering good cells in the brain. In which they begin in the brain, in what way they spread and how they grow will all bear upon how rapidly the cancer spreads. Other causes include the number of cells in the tumor at a specified point and the kill rate of appropriate prescription. Most causes of the brain tumors are unknown. However, some specialists stated that the cause of the disease is hereditary under the name of neurofibromatosis, while others expected that exposure to chemical and radiation is likely to be the cause of brain tumors (Lisei & Julitz, 2008). Brain tumor can be like brain forest fire, because it spreads on the outer perimeter along all

that stay in the center die often because lack of fuel (oxygen and nutrients from the blood). Figure 2.1 showed an example of the detection of brain tumor growth using computerized tomography (CT) which obtained from British Journal of Cancer (2002) by KR Swanson, EC Alvord and Murray. Based on Figure 2.1, the virtual human brain area is in the horizontal planes. The left side of Figure 2.1 describes the tumors diagnosis by CT-detectable tumors have an average diameter of 3 cm, whereas the right side of Figure 2.1 represents the same tumor of death. The CT scan is a series of designate images of the brain. The images were produced by a computer linked to an X-ray machine and indicating the high density zone of tumor cells. The elapsed time amid diagnosis and death for this virtual glioma is almost 158 days.

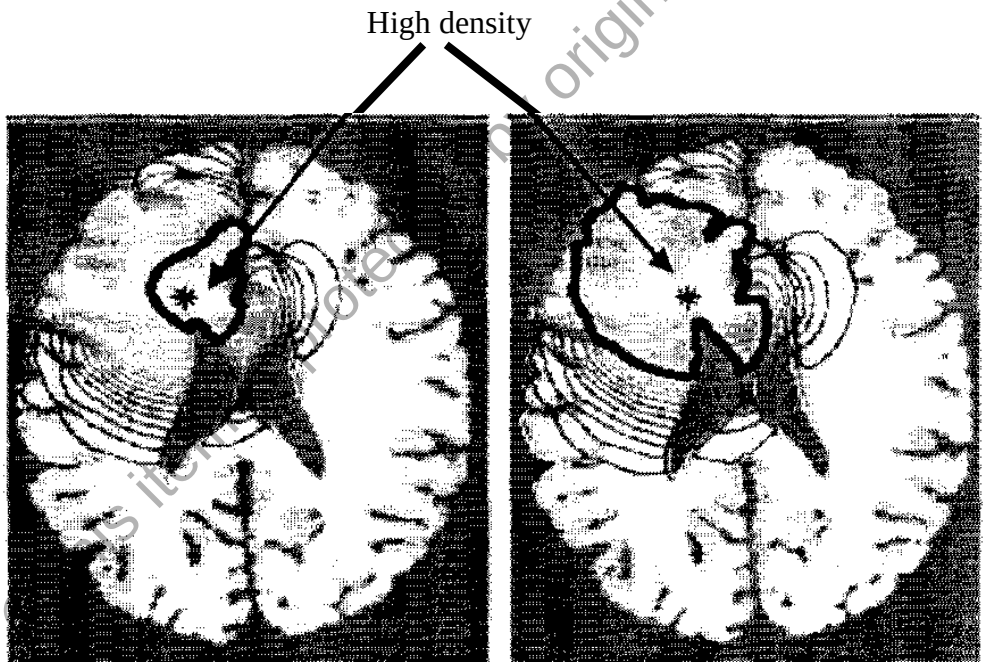

Figure 2.1: Detection of brain tumor growth using CT

Based on American Brain Tumor Association, 78,000 primary brain tumors cases were diagnosed in 2015. The amount consists 53,000 non-malignant and 25,000 primary malignant brain tumors. There were 4,600 children below 19 years old being

diagnosed with a primary brain tumors. There were around 700,000 people within the U.S. live with central nervous system tumors and primary brain tumors. In 2015, almost 17,000 people had lost their fight over central nervous system brain tumors and primary malignant brain tumors. In Malaysia, brain and spinal tumors are relatively rare compared to other tumors, which accounts only for 1.95% as reported by Goh et al. (2014). The statistics of the brain tumor from January 2009 till December 2012 has been recorded in Sarawak which the rough incidence of brain tumor was 4.6 % per 100 000 population per year with cumulative rate 0.5%. Meningioma (32.35%) was the most common brain tumor and come next by an astrocytoma (19.4%). A total of 468 patients were reported during the period of 2009-2012, of which 428 were brain tumors and 40 were spinal tumors. Among the patients of brain tumors, there were 247 females and 181 males. Primary brain and central nervous system tumors have more than hundreds different types. The survival with a primary brain tumor varies considerably via histology, age, tumor behavior and molecular markers. Age 59 was the average age at diagnosis for all primary brain tumors.

A brain tumor has been divided into two categories based on their origin and aggressiveness. For the aggressiveness, two groups have been classified i.e benign brain tumors (not cancerous) and malignant brain tumors (cancerous). Benign brain tumor grow very slowly and infiltrate into surrounding tissues. They are usually completely removed through surgery. On the other hand, malignant tumors grow rapidly and penetrate into the surrounding healthy tissues. Furthermore, their cells can go through cerebro-spinal fluid to other parts of the brain (Berger & Wilson, 1999). Malignant brain tumors are usually life-threatening and invasive, they are commonly called brain cancer. For the origin of brain tumor, it has been divided into two groups which are primary and metastatic. Primary brain tumors start from the brain. They usually occur in

kids and older adults. The metastatic of brain tumors are formed by cancerous cells which travelled to the brain from another part of the body. The majority of brain tumors of this type has metastasized to the brain from lung or breast cancer (De Angelis, 2001). They are the most common brain tumors and by nature malignant. Usually, higher grade In the next section,we will discuss about the gliomas which make up almost half of primary brain tumors diagnosed.

2.3 Gliomas

In the study of physics, biology and mathematics, cell growth is a phenomenon that has been studied (Wolpert et al, 2002). Uncontrollable growth of cell may be related to a extensive group of disease, which the cells turn into a lump or else cause illness. Gliomas is very popular malignant intrinsic primary tumors of the adult human brain (Larosz et al, 2015). The invasion is diffuse very forceful around the normal tissue. It made gliomas different from other tumors. Glioma is a kind of cancer of central nervous system that began in the brain or in the spine. Since it arise from glial cells, it was named a glioma. They were categorized by the World Health Organization such as oligodendroglioma, asytrocytoma, mixed oligoastrocytoma and ependymoma (Louis et al, 2007). Glioma cell migrates along blood vessels. Therefore, the glioma cell can extract nutrient from the bloodstream. Unlike other tumors, gliomas were normally high diffused. Figure 2.2 shows the glioma in the brain. Indeed, the results of experiment show that glioma cells could be recognized through central nervous system in seven days of tumor implantation in a rat's brain (Silbergeld & Chicoine, 1997). Gliomas was a dissimilar group of primary brain tumors that portion the ability of

penetrating diffusely throughout the brain, even though hardly metastasize over the central nervous system, (Westphal & Lamszuz, 2011; Kelly, 2010) .

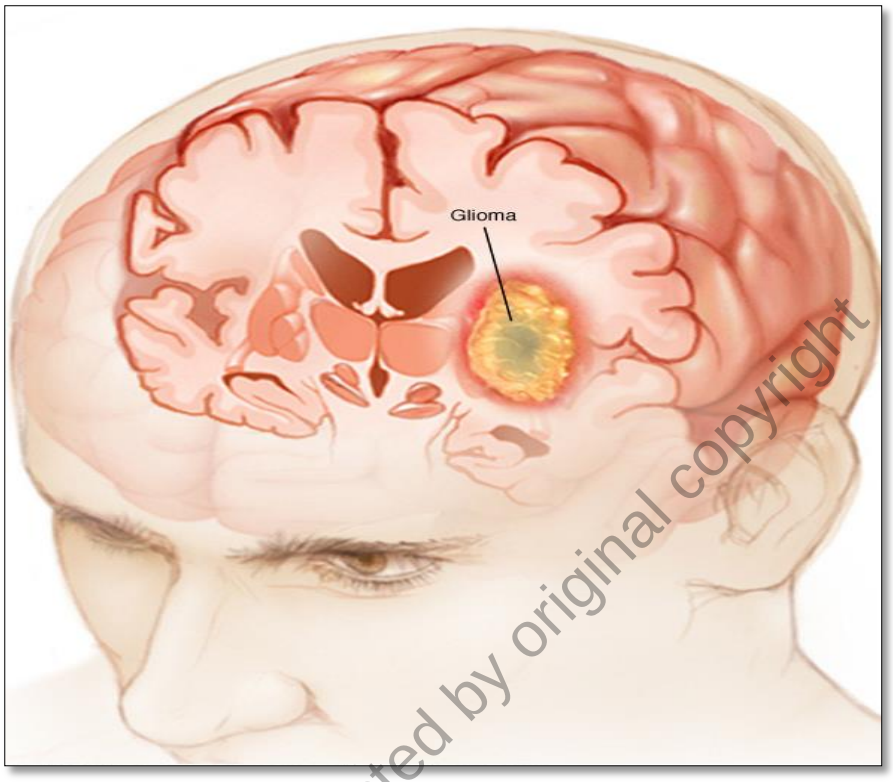

Figure 2.2: Glioma in the brain.

The diagnosis of patients with gliomas depend on numerous causes such as the histologic form and grade of malignancy, the patient's age and the degree of neurological functioning (Swanson, Bridge, Murray & Alvord, 2003). However, at least two aspects of the "grade of malignancy", which are invasiveness and net proliferationrate, are expected histologically but practically not once described specifically. Besides that, gliomas contains motile cell which can migrate as well as proliferate. An easy geometric expansion or exponential represents expansion of volume, which make it different from solid tumor. It nearly impossible to describe the growth rate being a typical volume-doubling time because of invasiveness. As Blankenberg et al (1995) stated, altough in the perfect situation whereas at least two

scans (CT, MRI) were analyzed at dissimilar times without treatment intervening. The boundary amongst tumor and normal tissue is not harsh and the amount of cell in the "normal tissue" is not determinable. As it is practically difficult either to learn the spatio-temporal infiltration or to measure the growth rate of gliomas which required to implement the results of decades on research of mathematical formulations of another cancers. It is obvious that new mathematical formulations are needed for gliomas.

2.4 Mathematical Models

Mathematical modeling of glioma is a widely discovered area with a great variety of mathematical models discovering multiple difficulties. A method to model glioma is used differential equations for the number of cells. There was a long history regarding the mathematical modeling of the tumor growth. Murray (1989) had introduced reaction diffusion model which made a big change in growth modeling. Diffusion and proliferation are the keys of biological behaviours that are considered in this model. Diffusion model tumor cell penetrate into the surrounding brain tissue whereas proliferation represents a reactive behavior which primary account for tumor cells growth and death. Isotropic diffusion model which let the tumor cells to diffuse similarly to whole directions with the equal speed for entire tissues has been used in early work (Cruywagen et al, 1995). Giese and Westphal (1996) proved that tumor cell moves slower in grey matter rather than white matter in their experimental results. Swanson, Alvord & Murray (2002) has included the experimental statement into the model of growth which multiply the tensors in white matter to a scaling factor.

In brain tumor, there are some equations and models that have been used to solve the growth of brain tumor such as parabolic equation, stochastic equation,

reaction-diffusion model and Swanson's glioma model. Pheng et al (2007) has used one dimensional parabolic equation in their research for the simulation of brain tumor growth which focussed on the implementation of parallel algorithm. In their research, the performance analysis measurement such as speed up, temporal performance, time execution, effectiveness and efficiency. Khairia, Wagdy & Ahmed (2015) has used the stochastic equation to measure the brain tumor growth in time and space, in order to understand the behavior of the tumor and the growth model. The reaction diffusion model has been applied to resolve the stability problem in the context of brain tumor prediction using anisotropic diffusion equation (Moseyabi, 2010). Özugurlu (2015) used the reaction diffusion model to inquire the stability state and the precisions of the numerical methods. The model solution has a lack of smoothness since the diffusion coefficient, D has a finite number of discontinuities. Swanson's glioma model is used in brain tumor response for radiation therapy (Rockne, Alvord, Rockhill & Swanson, 2009). Besides that, advantage of this mathematical model is the capability to detect response of tumor at any position throughout the therapy and virtually alter the treatment schedule and dose of delivery (Rockne et al, 2009).

For this study, the model by Swanson, Alvord and Murray (2000) will be used. The model is given by

$$\frac{\partial c}{\partial t} = \nabla.\left(D(x)\nabla c\right) + \rho c. \tag{2.1}$$

To solve the second problem, equation (2.2) will be used which is

$$\frac{\partial c}{\partial t} = \nabla.\left(D(x)\nabla c\right) + \rho c\left(1 - \frac{c}{c_{\max}}\right). \tag{2.2}$$

From equations (2.1) and (2.2), $c(x,t)$ is the concentration of cells at any position x and time t, ρ is the unit of growth rate per day and signifies the net rate of growth of

abnormal cells, together with proliferation, loss and death, while $D(x)$ represents the units of cm^2 per day and denotes the diffusion coefficient of cells in brain tissue. We note that $D_{(x)} = D_g$ (constant for x in grey matter) and $D_{(x)} = D_w$ (constant for x in white matter), $c_{\max}$ is the maximum carrying capacity and ∇ represents the spatial gradient.

A simple Fickian diffusion (Murray, 1993) has described the diffusion term *D* as the active migration of the glioma cells which the cells stir from regions of upper density to lower density. It feast diffusely over the brain because gliomas are extremely invasive. This make the expectation of life from 6 to 12 months (Alvord Jr, 1995) to a very forceful level of gliomas identified as glioblastoma multiforme (GBM). Tumor cells are assumed to grow exponentially.

2.5 Numerical Method

In the partial differential equation (PDEs), there are some methods that can be used to solve the problems of brain tumor growth such as finite element method and finite difference method. Finite element method allows any solution domain to be divided into several simple subdomains. This is the basic concept of finite element method. Therefore, an easy form of solution in every finite element method can be assumed so that the estimated answer of the problem in the complete domain can be established (Rao, 2002). Finite element method has been used to simulate the invasion of glioblastomas multiforma (GBM) in the brain and its mechanical interaction with the invaded structures (Clatz et al., 2005).

Nakamura (1993) stated that finite difference method is a typical and direct technique to solve the PDE numerically. It is a well-established and conceptually

modest method which needs a point-wise estimation to the main equation. Explicit, implicit and Crank-Nicolson methods are finite difference method. Explicit method is the simplest method and has three basic operators in its discretization parts, i.e forward, backward and central approximations. This method has been used in the design of a platform for discretizing the parabolic equation (Pheng et al., 2007). 1D parabolic equation concerning the brain tumor growth has been presented. Based on the results, Crank-Nicolson and fully implicit approaches are more suitable to describe the tumor growth rather than explicit method. Finite difference method also has been used to solve the stability effect of brain tumor growth (Moseyabi, Cobzas, Jagersand & Murtha, 2010). Besides that, Islam et al (2011) has used the same method in order to solve advection diffusion equation which describes the evolution of brain tumor growth. Therefore, finite difference method will be used in this study since it is easy to carry out (Moseyabi, 2010) and the discretization of the 1D reaction diffusion equation for detecting brain tumor growth is discussed in the next chapter.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Introduction

This chapter discusses about the numerical techniques to solve the 1D reaction diffusion equation in detecting the brain tumor growth. The numerical schemes which used for the discretization process is explicit methods.

Figure 3.1 shows the methodology for the method's development in detecting the brain tumor growth. Firstly, the discretization process of 1D reaction diffusion equation will be done. Secondly, the discretization of reaction diffusion equation will be carried out by using explicit method for the brain tumor growth detection. Third process is to perform the numerical simulation on 1D reaction diffusion equation. All numerical algorithms must be correctly implemented in the MATLAB to get the numerical approximation of the brain tumor growth.