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SURVIVAL PERIODS FOR VARIOUS GRADES OF GLIOMAS IN HUMAN BRAIN CANCER BY USING MATHEMATICAL MODEL

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Abstract

Cancerous tumors or neoplasms originate from the mutation of one or more cells which usually undergo rapid uncontrolled growth thereby impairing the functioning of normal tissue. There are many different cancers and their own characteristics we expect increased boundary effect and more complex patterns of invasion due to heterogeneous distribution of gray matter and white matter. We discuss about model application to the human brain geometry and investigate the implication of heterogeneous diffusion on the spread of an introduced virtual tumour. In human brain we are interested in the variation in parameter values in while and gray matter regions. We use Fisher Kolomogroff approximation CT scans parameter values to determine the velocities of the tumour front in gray matter and white matter. We determine and compare a five-fold difference in the diffusion coefficient in grey matter and white matter and also survival periods (times) for various grade of gliomas at three positions of white and gray matter.

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1. Introduction

Stochastic Processes:

Random Process: Consider a random experiment with a sample space S. If a time function $X(t, s)$ is assigned to each outcomes $s \in S$ and where $t \in T$, then the family of all such functions denoted by $\{X(t, s)\}$, where $s \in S$, $t \in T$ is called a random process.

In other words a random process is a collection of random variables together with time. A random process is called stochastic process.

Markov Process: Markov process is a random process in which future behavior of the process depends only on the current state and not on the states in the past.

$P\{X(t) \le x / X(t_1) = x_1,\ x(t_2) = x_2 \ldots X(t_n) = x_n\}$ i.e.

$P\{X(t) \le x / X(t_n) = x_n\}$.

A discrete parameter Markov process is called Markov Chain. The Markov Chain as follows,

If $P\{X_n = a_n / X_{n-1} = a_n, X_{n-2} = a_{n-2}, \ldots, X_0 = a_0\} \Rightarrow P[X_n = a_n / X_{n-1} = a_{n-1}]$

for all 'n', then the process X_n; $n = 0, 1, 2, 3, \ldots$ are called as Markov Chain.

Here $a_1, a_2, a_3, \ldots$ are called the states of the Markov chain.

The conditional probability $P[X_n = a_j / X_{n-1} = a_i]$ is called the one step transition probability from state a_i to state a_j at the n^{th} step (trial) and is denoted by $P_{ij}(n-1, n)$.

If $P_{ij}(n-1, n) = P_{ij}(m-1, m)$, then the markov chain is called the homogeneous markov chain (or) the chain is to have stationary transition probabilities. When the markov chain is homogeneous, the one step transition probability, is denoted by P_{ij}. The matrix $P = \{P_{ij}\}$ is called (one step) Transition Probability Matrix (TPM).

Regular Matrix: A stochastic matrix 'P' is said to be a regular matrix of P^m (for some +ve integer m) are +ve. A homogeneous Markov chain is said to be regular if its tpm is regular.

2. Condition for Steady State Distribution

If P is the tpm of the regular markov chain and $\Pi = (\Pi_1, \Pi_2, \Pi_3, \ldots, \Pi_k)$ is the steady state distribution, then $P = \Pi$ and $\Pi_1 + \Pi_2 + \ldots + \Pi_k = 1$.

In 3×3 matrix then $\Pi = (\Pi_1, \Pi_2, \Pi_3)$, $\Pi P = \Pi$; $\Pi_1 + \Pi_2 + \Pi_3 = 1$.

In 2×2 matrix then $\Pi = (\Pi_1, \Pi_2)$; $\Pi P = \Pi$; $\Pi_1 + \Pi_2$

⇒ When all the entries of a tpm are positive, (i.e.) if the tpm is regular and of the form $P = \begin{pmatrix} 1-a & a \\ b & 1-b \end{pmatrix}$

(i) $\Pi = P^{(n)} = \frac{1}{a+b}\left[\begin{pmatrix} b & a \\ b & a \end{pmatrix} + (1-a-b)^n \begin{pmatrix} a & -a \\ -b & b \end{pmatrix}\right]$

(ii) $\Pi = \left(\frac{b}{a+b}, \frac{a}{a+b}\right)$

⇒ If the tpm of a chain is a stochastic matrix, then the sum of all elements of any row is equal to 1.

3. Cancer

A tumour is a mass of tissue that's formed by an accumulation of abnormal cells.

Brain Cancer:

Tumors in the brain can be malignant or benign and can occur at any age. Only malignant tumors are cancerous. Primary brain tumors cancer initially forms in the brain tissue. Secondary tumors cancers that have spread to the brain tissue (metastasized) from elsewhere in the body.

Most of the brain tumors develop from the cells that support the never cells of the brain called glial cells. A tumor of glial cells is a gliama. A tumour

of the pituitary gland is called an adenoma. A tumor developed from the covering of the brain (the meninges) is called a meningioma.

Tumors growing from the nerves entering the brain are called neuromas. A vestibular Schwannoma (also sometimes called an acoustic neuroma) is a tumour growing on the nerve that controls balance and hearing.

Stage of Brain Cancer: A brain tumor is the uncontrolled growth of damage cells in the brain. This growth also spreads to the spinal column causing more harm to the body.

The stages are,

Stage Zero	It is the early stage of brain cancer
Stage One	Although the cells are already infected they appear normal. This is because it is hard to see the cancer cells at this stage. Surgery is the most preferred method of treating stage one cancer.
Stage Two	Although the cancer cells are growing at a very high rate in the stage the cancer is still curable or could be treated.
Stage Three	In this stage the already damaged cells are growing rapidly.
Stage Four	This is scariest cancer stage. This is because the disease has already spread to almost all parts of the body. this is it is hard to treat stage four.

Symptoms: Symptoms vary depending on the tumour type, size and location in the brain. General symptoms include:

- Headaches that tend to worsen in the morning
- Seizures
- Difficulty walking
- Speech problems
- Abnormal eye movement
- Weakness on one side of the body

Types: More on the types of cancer is that they are classified depending on the origin of the tumour.

Ependymoblastoma: This is a type of cancer in young children and infants.

Astrocytoma: Astrocytes are types of brain cells. A tumour arising in the supportive cells of the brain.

Glioblastoma: This is the Second type of brain cancer.

Medulloblastomas: This is another type of brain cancer found in children. It is originate in the cerebellum before spreading to other parts of the body.

Pineoblastomas: This type of cancer occurs in the pineal gland. This refers to the pine shaped gland in the vertebrae part of brain.

Brain Tissue Types: The brain consists of two of tissue: (1) Gray Matter (2) White Matter Gray Matter is composed of neuronal and glial cell bodies that control brain activity while the cortex is a coat of gray matter that covers the brain. White Matter is fibre tracts are myelinated neuron axon bundles located throughout the inner regions of the brain.

Corpus Callosum: Corpus callosum is a thick band of white matter fibers connecting the left and right cerebral hemispheres of the brain. To estimate diffusion co efficient from the experimental data, we use the Fisher-Kolmogroff approximate. We know that the travelling wave speed is given by $v = 2\sqrt{\rho D}$, where $\rho = (\text{time}^{-1})$ represents the net rate of growth of cells including proliferation and death (or less). $D = \overline{D}$ (or) $(\text{distance}^2/\text{time}^{-1})$ is the diffusion coefficient of cells in brain tissue and we consider $v = \frac{\bar{r}}{\bar{t}}$ be the velocity of the profile front, $D = \frac{v^2}{4\rho}$. We need to determine the growth rate of the tumour cells. Here we use this Fisher-Kolmogroff approximate with experimental results.

The Fisher-Kolmogroff estimate implies that a very low growth rate with a large linear velocity gives very high estimates for the diffusion rate for the tumor cells in both white and gray matter with in the right hemisphere the margin of detectable tumor moved about 1.5cm, i.e., average speed $v = 8.0 \times 10^{-3}$cm/day for growth rate $\rho = 0.012$/day. The asymptotic from of the radial travelling wave of the axisymmetric Fisher-Kolmogroff equation

$$\bar{r}^* = 2\sqrt{D\rho}\bar{t}\sqrt{1-\frac{1}{\tau\bar{t}}\ln\left(4\pi D\bar{t}\,\frac{\bar{c}^*}{N_0}\right)} \approx 2\sqrt{D\rho}\bar{t} \quad \text{for} \quad t \quad \text{large}, \quad D = \frac{v^2}{4\rho}$$

$=1.3\times10^{-3}\text{cm}^2/\text{day}$ and if the tumor is identified when it has a radius $\bar{r}_{\text{detect}}$ and if tumour is fatal when it has a radius $\bar{r}_{\text{lethal}}$.

$$\text{Survival time} = \bar{t}_{\text{lethal}} - \bar{t}_{\text{detect}} = \frac{1}{\sqrt{D\rho}}(\bar{r}_{\text{lethal}} - \bar{r}_{\text{detect}}).$$

Here D and ρ are both important parameter in determining survival time, increasing either D and ρ decrease survival time. The average radius is identified is 1.5cm and lethal 3.0cm these are only average values observed clinically. The three tumour sites are

position (1): an inferior fronto – parietal tumor.

position (2): a superior fronto – parietal tumor.

position (3): a temporal lobe tumor.

At each of these locations we consider the four tumor grades representing 5-fold variations in the growth rate ρ and the diffusion coefficient D. High grade (high ρ, high D), Intermediate grade (high ρ, low D or low ρ, high D), Low grade (low ρ, low D).

Table (1). Survival periods for various grades of gliomas at different sites in the human brain. The diffusion coefficient in white matter $Dw = 5Dg$.

Grade	Growth rate ρ (per/day)	Diffusion coefficient Gray matter Dg(cm2/day)	Survival periods t_s (day) (Position) $P1$	$P2$	$P3$	$\bar{r}_{\text{lethal}}$	$\bar{r}_{\text{detect}}$ Fixed (cm)
HH	1.2×10^{-2}	1.3×10^{-3}	109	138	173	P1-2.808 P2-3.140 P3-3.560	1.5
		6.5×10^{-3}	157	186	233		
HL	1.2×10^{-2}	1.3×10^{-4}	398	497	582	P1-1.997 P2-2.12 P3-2.227	1.5
		6.5×10^{-4}	178	222	260		
LH	1.2×10^{-3}	1.3×10^{-3}	55	259	347	P1-1.569 P2-1.824 P3-1.934	1.5
		6.5×10^{-3}	25	116	155		
LL	1.2×10^{-3}	1.3×10^{-4}	1097	1375	1727	P1-1.93 P2-2.043 P3-2.182	1.5
		6.5×10^{-4}	492	615	775		

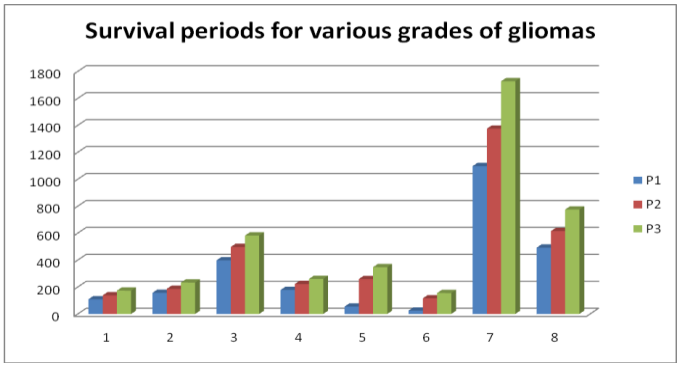
By using condition for steady state distribution, we calculated survival periods for various grades of gliomas at different sites in the position 1, position 2, position 3 in the human brain given table 1 and table 2 is the diffusion coefficient in white matter $Dw = 5Dg$.

Table 1.

	$\Pi_1(\rho)$	$\Pi_2(D)$
P1	94%	6%
P2	8%	2%
P3	8%	2%

Table 2.

	$\Pi_1(\rho)$	$\Pi_2(D)$
P1	9%	90%
P2	7%	2%
P3s	7%	2%



4. Discussion

Survival periods for grade of gliomas at various position 1, position 2, position 3 are given by combination of High grade and Low grade in ρ and D, if ρ and D in high grade and low grade in survival periods of three positions will be 94% and 6%,8% and 2%,8% and 2%. At the same side we found the survival periods for grade of gliomas, the diffusion coefficient in $Dw = 5Dg$ for each tumor grade, if ρ and D in high grade and low grade in survival periods of three positions will be 9% and 90%,7% and 2%,7% and 2%.

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