Oxygen Distribution in Tumour Slice

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Abstract-*Multi cell tumour spheroids were used in cancer related experiments to find growth characteristics of tumours. By using Mathematical models of tumour growth, unknown tumour growth characteristics can be predicted quantitatively. For studying tumour growth in non spherical form, a thin slice model by using diffusion theory is tested for Oxygen distribution inside the slice of the tumour*

Keywords: Non Spherical Tumour, Oxygen concentration in Tissue, Oxygen distribution in non spherical tumour, Multi cell Tumours.

I. INTRODUCTION

Cancer is one of the most common life threatening diseases of the present world and is a major cause of death all over the world. More than a million Indians suffer from cancer and a large number of them die due to cancer annually. Cancer usually appears as a lump, an unwanted and abnormal growth of the tissue called Tumour. Cancer tumours can develop at any part of the human body. Finding treatment strategies to combat the cancer is the basic aim of the cancer research. Judah Folkman and Hochberg (1973) conducted experiments using multi cell tumour spheroids to find growth characteristics of the tumours. During their experiment, the multi cell tumour spheroids gone through three different stages of growth. In the last stage, a necrotic region consisting of dead cells was formed in the centre of the spheroid due to non availability of Oxygen to the innermost cells of tumour spheroid. Mathematical models were developed to understand the tumour growth. Mathematical models help us to study the phenomenon without going for the actual experiment by assigning values to the variables of the model. In this paper, distribution of Oxygen is studied in tumour by using the mathematical concept of diffusion considering a model of tumour slice.

II. LITERATURE REVIEW

Growth of Multi cell tumour spheroids were examined by Burton A.C. (1966), Judah Folkman and Hochberg (1973), R.M. Sutherland (1974), H.P. Greenspan (1973), Freyer J.P (1988). Burton A.C., developed a diffusion model which examined the distribution of Oxygen in spherical tumour and showed that the growth of the solid tumours not obey exponential law of growth but follows Gompertzian relation in which growth constant itself declines exponentially with time. The model given by Burton A.C. also predicted critical tumour radius at which necrosis in Central spot will appear. According to Judah Folkman the dormant phase of the tumour spheroid begins when the spheroid ceases to expand further. In Multi cell tumour spheroid experiments, it is observed that both Oxygen and Glucose are rapidly consumed by most tumour cells [8]. H.P Greenspan extended Burton models by introducing surface tension among the living cancer cells in order to maintain solid mass. A.S. Deakin study is related to effect of non uniformity of oxygen consumption on viable rim thickness.

III. DIFFUSION MODEL IN SLICE OF THE TISSUE

Diffusion of Oxygen in a non spherical tumour tissue can be studied by considering a thin slice of the tumour of thickness Δx by exposing it to the different concentrations of Oxygen through nutrient medium in the culture. When the flow of Oxygen takes place through the slice, a certain amount of Oxygen is absorbed by the tissue and the remaining Oxygen comes out from the slice. For our convenience if the process is considered along x - axis with two end points of the slice as x and $(x+\Delta x)$ which shows thickness of the slice as Δx . It can be represented by the following diagram.

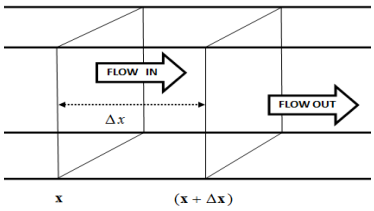

Figure1. Diagrammatic representation of Oxygen flow in slice of the tumour tissue

Consider the slice has a cross sectional area α and the concentration of Oxygen be $C(x)$. Let the rate of consumption of Oxygen per unit volume per unit time in the slice is A and the Diffusion coefficient in the tissue is D. The amount of Oxygen flowing into the volume of the slice at x per unit time must be equal to the amount of Oxygen flowing out of the slice at $(x+\Delta x)$ and the amount of Oxygen

consumed in the volume of the slice per unit time. By the law of conservation, $In = Out + Consumed$. According to Fick's law, the amount Of Oxygen flowing into the slice at x can be taken as $\left[-D\frac{dC}{dx} \right]_x \alpha$ and Oxygen flowing out from the slice can be taken as $\left[-D\frac{dC}{dx} \right]_{(x+\Delta x)} \alpha$, by assuming the slice is full of live cells, the consumption of Oxygen in the slice will be $A.\alpha.\Delta x$. By applying mean value theorem, this will lead to the governing equation of Oxygen diffusion in the slice of the tissue $\frac{d^2C}{dx^2} = \frac{A}{D}$. Solving the differential equation, we will get Oxygen concentration equation in the slice of the tissue as below.

$$C(x) = \frac{Ax^2}{2D} + \left(\frac{C_L - C_0}{L} - \frac{AL}{2D} \right) x + C_0$$

The equation represents concentration of Oxygen in the tissue at a distance x between $x = 0$ and $x = L$. C_0 is initial Oxygen concentration at $x = 0$, C_L is concentration of Oxygen at a distance $x = L$. $C(x)$ is concentration of oxygen at a point x between $x = 0$ and $x = L$ $(0 < x < L)$.

V.OXYGEN DISTRIBUTION INSIDE THE SLICE

The live cells of the tissue absorb Oxygen, and by assuming the more distance we move away from the point $x = 0$, the concentration levels of the Oxygen in the slice of the tissue goes down. i.e. $C_L < C_0$ and $\left(\frac{C_L - C_0}{L} \right)$ will be negative. Due to negative term in the equation, we can easily observe from the equation that the Oxygen concentration in the slice is directly proportional to the initial concentration C_0 . The higher concentrations of Oxygen in the nutrient medium in the initial stage outside the slice of the tissue will make differences in concentrations of Oxygen inside the slice of the tissue at different locations. The behaviour of the equation can be studied by giving arbitrary values to x in between $[0, L]$. MATLAB program is used to obtain the graph of the equation with different values for A, D, C_0, C_L and L . $A = 5, D = 1.75, C_L = 200$ & $L = 25$.

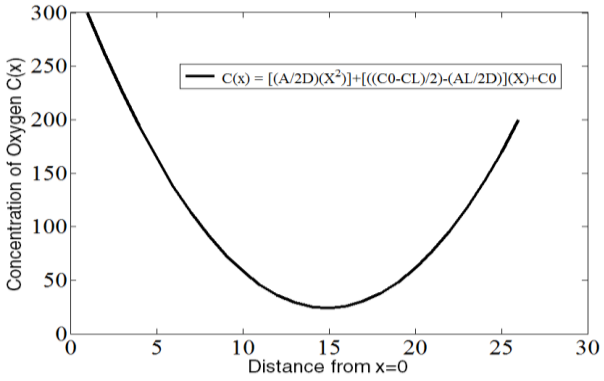

Figure2. Graph of Oxygen concentrations in slice of the tissue at different points of x .

To study further about lowest Oxygen concentration levels in between the points $[0, L]$ and to check the effect of Oxygen concentration at end point L along with parabolic behaviour of the graph, MATLAB program is used with different Oxygen concentration values at a fixed point L.

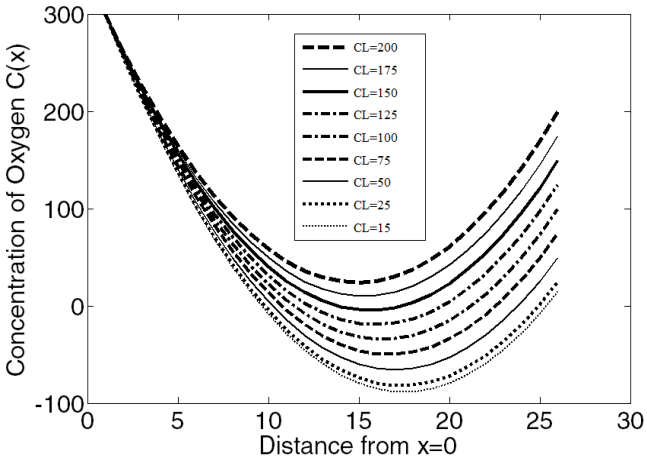

Figure3. Graph of Oxygen distributions in slice of the tissue for different values of C_L at a fixed point L .

By assuming due to any other internal factors inside the slice of the tissue if $C_L > C_0$, the existence of lowest Oxygen concentration level and distribution of Oxygen at different points can be studied by from the graph giving large values to C_L in the equation.

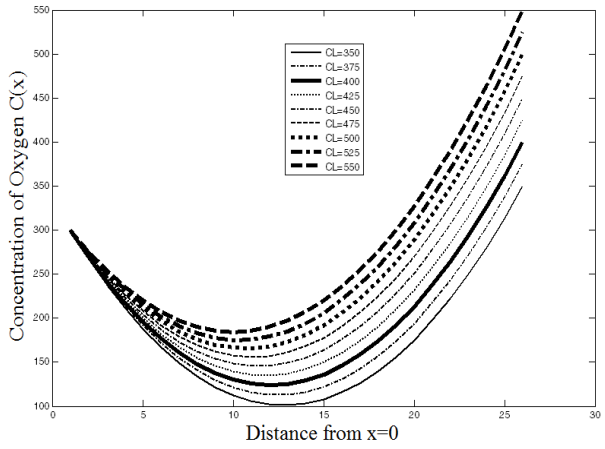

Figure4. Graph of Oxygen distributions in slice of the tissue for different large values of C_L .

But interestingly another phenomenon is observed when C_L is very high. The graph is no more a parabolic shape but it is taking exponential shape with continuously increasing Oxygen concentration inside the tissue with lowest value at the initial place $x = 0$. The effect can be observed from the following graph.

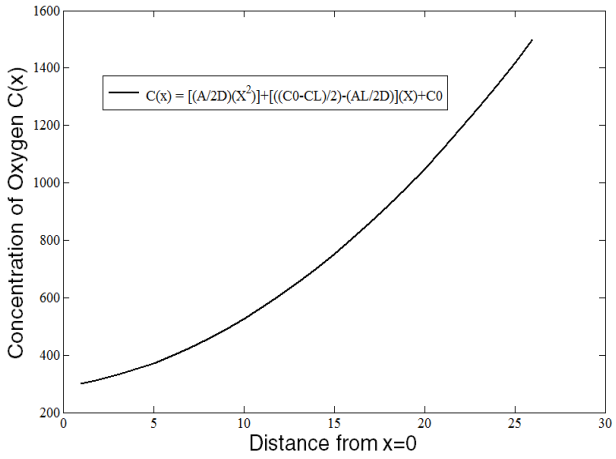

Figure5. Graph of Oxygen concentrations inside slice of the tissue with very high value of C_L .

The effect of different Oxygen consumption rates on the equation can be seen from the following graph.

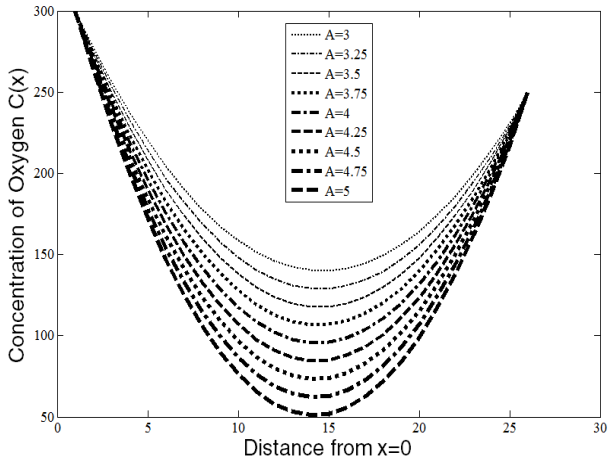

Figure.6 Graph of Oxygen distribution in slice of the tissue for different Oxygen consumption rates.

Similarly the effect of different diffusion coefficients in the equation can be seen with the following graph for different diffusion coefficients.

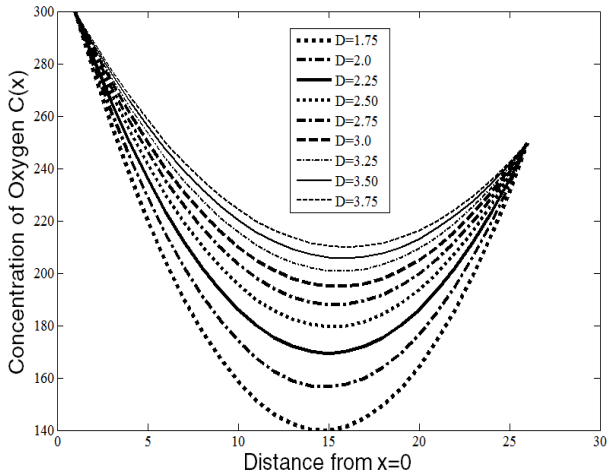

Figure.7 Graph of Oxygen distribution in slice of the tissue for different diffusion coefficients

From Figure 6, it is clear that for higher values of Oxygen consumption rates A, the Oxygen concentration levels fell down inside the slice of the tissue and from figure 7, the Oxygen concentration levels gone up with higher diffusion coefficients D. The above effect of both parameters can be seen in the following graph.

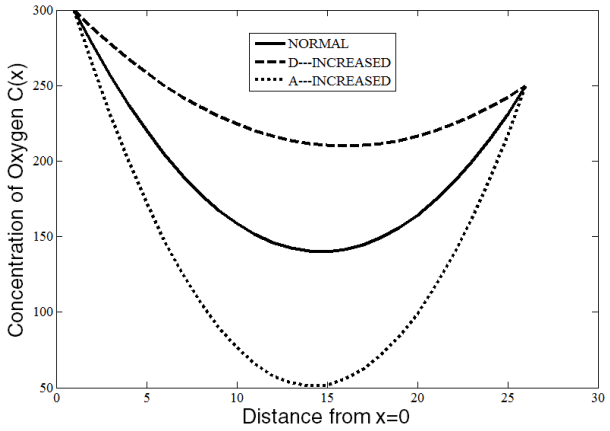

Figure.8 Graph of Oxygen distribution in slice of the tissue for increased diffusion coefficient and increased Oxygen consumption rates along with normal condition values.

From the figure 8, we can conclude that increasing Oxygen concentrations inside the slice of the tissue are due to respective increase in value of diffusion coefficient and decreasing Oxygen concentrations are due to increase in value of Oxygen consumption rate by keeping other values constant. The mixed effect of all the variables can be studied by giving specific values to the variables C_0, C_L L, A and D . And all the parabolic shape of the graphs is direct effect of the point L and Oxygen concentration at that point. If the distance is decreased to nearly half and Oxygen concentration at this point is assumed to be half, the graphs never take a parabolic shape. The effect can be visualized in the following graph with three situations.

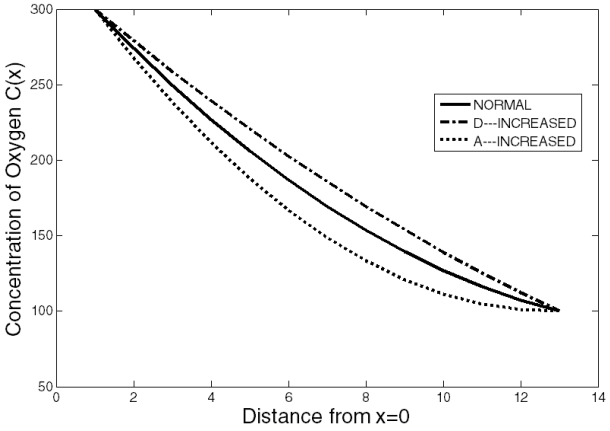

Figure.9 Graph of Oxygen distribution in slice of the tissue for increased diffusion coefficient and increased consumption rate along with normal condition values in small range of L

VI. CONCLUSIONS

1. From figure2 it is clear that the concentration of Oxygen is not decreasing as it is moving away from the initial point but it is taking parabolic shape by taking lowest value at a point in between $[0, L]$ .The reasons for this particular behaviour could be the effect of Oxygen flow through the wide open cross sectional area of the slice. Above observation leads us to conclude that the growth of the tumors is dependent on the surface area of the initial tumor exposed to growth supportive environment. The growth of the tumour can be restricted by making minimal exposure around the tumour depending upon the location of the tumour.

2. The graph in figure3 clearly shows that irrespective of the concentration levels of Oxygen at the end point L , the Oxygen concentration is lowest at some point in between $[0, L]$ forcing the graph to acquire parabolic shape. It can also be observed from the graph that the lowest concentration level is not exactly at a fixed point but it is changing as the concentration level at the end point L is changing. The Oxygen concentration level is sliding towards right side as C_L is decreasing. In the graph we can see the lowest Oxygen concentration is even negative in some cases which are absurd and meaningless in this situation. The negative values are purely due to very low values of C_L . So we can conclude that the Oxygen concentration at the point L cannot be as low as we assigned but there could be a certain limit beyond which we cannot expect such a lowest value, depending upon the initial Oxygen concentration values of C_0

3. When Oxygen consumption rates were increased, the Oxygen concentration inside the slice decreased and increase in diffusion coefficients increased the concentration levels inside the slice.

4. When L (the distance from initial point) is very small, the graph never takes a parabolic shape. The point of least concentration level is not constant and it is dependent on the value of L.

REFERENCES

[1] A.C. Burton, Rate of growth of solid tumours as a problem of diffusion, Growth 30(1966), 157-176.
[2] A.S. Deakin, Model for the growth of a solid in vitro tumor, Growth 39(1975), 159-165
[3] Folkman J, and M. Hochberg, (1973), Self regulation of growth in three dimensions. J. Exp .Med 138:745-753.
[4] Freyer JP, Tustanoff E, Franko AJ ,Sutherland RM, In situ Oxygen consumption rates of cells in V-79 multi cellular spheroids during growth. J Cell Physiol (1984) Jan; 118(1):53-61.
[5] H.P. Greenspan, Models for the growth of a solid tumor by diffusion, Stud.Appl.Math.52 (1972), 317-340.
[6] H.P. Greenspan, On the growth and stability of cell cultures and solid tumors, J. Theor. Biol.56 (1976), 229-242
[7] Sutherland R.M, and R.E Durand (1976). Radiation response of multi cell spheroids - an in vitro tumor model. Curr.Top.Radiat Res 11:87-139.
[8] James P. Freyer and Robert M. Sutherland, Regulation of Growth saturation and Development of Necrosis in EMT6/RO Multi cellular Spheroids by the Glucose and Oxygen Supply. Cancer Research 46, 3504-3512.
[9] Spheroids in Cancer Research-Methods and Perspectives. (Acker, H., Carlsson, J., Durand, R., Sutherland, R.M), Springer-Verlag (1984)

Note: Above article is a part of the research work carried out for PhD course curriculum under Osmania University in Dept of Mathematics with title Theoretical study of problems in life sciences and Medicine.