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Analytical Ballpark Solution of the Glioblastoma Tumor Cells Growth in Homogeneous Medium

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ABSTRACT

Glioblastoma is high grade-IV malignant tumor, where a large part of tumor cells are reproducing and dividing at any given time. The essential model considers the evolution of the Glioblastomatumor cells population which mostly governed by the proliferation and the diffusion. Kamal Variational Iteration Method is developed. It gives fast convergent consecutive approximations without using any restrictive assumptions which may change the physical behaviour of the problems. Kamal Transform is a new advent of an integral transform derived from classical Fourier Transform to solve the linear initial value problems. KVIM is established to solve the models.
Aim of this research is to thrash out the current developments of the methods to crack the mathematical modelling of Glioblastomatumor cells growth and it might be open the doors for improvement.

Keywords:
GlioblastomaTumor, Homogeneous Medium, Kamal Variational Iteration Method

Introduction

Glioblastoma is the most common high grade-IV cancerous primary brain tumor which mostly occurs in adults and rarely occurs in offspring. Glioblastoma belongs to a group of brain tumors known as Glioma. They grow in a glial cell, a type of brain cell, known as Glioblastoma, are malignant high grade-IV tumors, where a large part of tumor cells are reproducing and dividing at any given time. [W1-W2]

Brain as a whole consists of two types of tissues: White matter and Gray matter. Glioblastoma grows faster in White matter than the Gray matter.

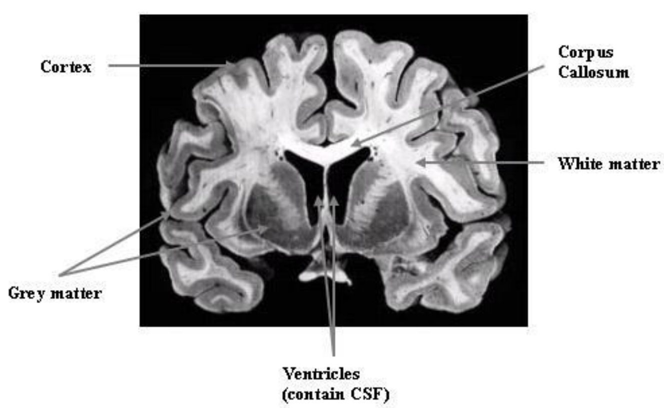

Fig.1 Schematics Diagram of Internal Part Brain

To solve the mathematical models of the GlioblastomaTumor cells growth in homogeneous medium, when early cancer cells are known and unknown. To solve these models we used the

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combination of Variational Iteration Method and the new onset transform - Kamal Transform - Kamal Variational Iteration Method.

Kamal Transform is denoted and defined as, [17]

$$K\left[g(t)\right] = G(v) = \int_0^\infty e^{-\frac{t}{v}} g(t)\,dt \;; t \geq 0, m_1 < v < m_2$$

.

2. Kamal Variational Iteration Method (KVIM):

To exemplify the design of Kamal Variational Iteration Method, Consider the general differential equation, as

$$L\left[P(X,T)\right] + N\left[P(X,T)\right] = h(X,T) \quad (1)$$

According to the Variational Iteration Method, the correctional function of (1) is, [5,7]

$$P_{n+1}(X,T) = P_n(X,T) + \int_0^T \lambda(X,\tau)\left[L\left[P_n(X,\tau)\right] + N[\overline{P}_n(X,\tau)] - h(X,\tau)\right]d\tau, n \geq 0 \quad (2)$$

Where λ is a general Lagrange Multiplier, which can be identified optimally via variationaltheory. $\overline{P}_n$ is a restricted variation. i.e. $\delta\overline{P}_n = 0$. Lagrange Multiplier λ can be obtain using integration by parts of (2). Kamal transform is used here to find it.
We get the iteration formula for KVIM as,

$$\left[P_{n+1}(X,T)\right] = K\left[P_n(X,T)\right] + K\left[-T\right] \cdot K\left[L\left[P_n(X,T)\right] + N\left[P_n(X,T)\right] - h(X,T)\right] \quad (3)$$

3. Parameter Estimation:

- In realistic mathematical model, parameter estimation is crucial. Generally high grade Gliomas doubles in 1 week while low grade Gliomas in 12 months (Alvord & Shaw 1991). For high grade Astrocytomas doubling time is 2 months for $\rho = 0.012$/ per day. Normal glial cells have low diffusion rate [6], while Glioma cells have high diffusion rates [2]. It has been observed that in Rat Glioma cells in Vitro that average linear velocity is 12.5 mm/h, while in Vivo average linear velocity is 4.8 mm/h [2].
- Fisher's approximation relate linear velocity v of a detectable tumor margin with the proliferation rate ρ and a random walk diffusion coefficient D defined as $D \approx \frac{v^2}{4\rho}$ [9,10].
- Form CT scans, it has been observed that the speed of advance of the tumor margin across the corpus callosum (white matter) is two to three times as fast as that in predominantly grey matter. i.e. $v_w > 2.2\, v_g \quad D_w > 5D_g$.[9,10]
- Throughout our simulation we use $v_w = 2.2\, v_g \quad D_w = 5D_g$.
- Tumor cells growth rate and diffusion rate is important to check the future scenario of the patient. There are three types of grade: High grade (HH: High ρ, Low D), Intermediate Grade (HL: High ρ, Low D & LH: Low ρ, High D) & Low Grade (LL: Low ρ, Low D).[9,10]

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4. Mathematical Models of GlioblastomaTumor Cell Growth in Homogeneous Medium

Fundamental model for the Reaction Diffusion Equation is used here as,

$$\frac{\partial P}{\partial T} = D\nabla^2 P + \rho P \quad (4)$$

This model gives realistic conformity with the results of CT scans. So results are useful to predict the survival times under the various treatments [10]. Kamal Vriational Iteration Method is used to solve (4). Two parts are considered as spread of early cancer cells are known and unknown.

Case:1 When spread of early cancer cells are unknown:

Considering the one dimensional GliomablastomaTumor Cells growth model with constant diffusion and constant growth rate at any fixed position occurs in Homogeneous Medium as either in White Matter or in Gray Matter,

$$\frac{\partial W}{\partial T} = D\frac{\partial^2 W}{\partial X^2} + \rho W \; ; W(X,0) = W_0 \quad \text{(In White Matter) [9,10]} \quad (5)$$

or $$\frac{\partial G}{\partial T} = D\frac{\partial^2 G}{\partial X^2} + \rho G \; ; G(X,0) = G_0 \quad \text{(In Gray Matter) [9,10]} \quad (6)$$

Applying KVIM, we get the iterations as,

$W_1(X,T) = W_0[1+\rho T]$ & $G_1(X,T) = G_0[1+\rho T]$

$$W_2(X,T) = W_0\left[1+\rho T+\frac{\rho^2T^2}{2!}\right] \; \& \; G_2(X,T) = G_0\left[1+\rho T+\frac{\rho^2T^2}{2!}\right]$$

$$W_3(X,T) = W_0\left[1+\rho T+\frac{\rho^2T^2}{2!}+\frac{\rho^3T^3}{3!}\right] \; \& \; G_3(X,T) = G_0\left[1+\rho T+\frac{\rho^2T^2}{2!}+\frac{\rho^3T^3}{3!}\right]$$

$\vdots$

$$W_n(X,T) = W_0\left[1+\rho T+\frac{\rho^2T^2}{2!}+\frac{\rho^3T^3}{3!}+\ldots+\frac{\rho^nT^n}{n!}\right] = W_0e^{\rho T} \; \&$$

$$G_n(X,T) = G_0\left[1+\rho T+\frac{\rho^2T^2}{2!}+\frac{\rho^3T^3}{3!}+\ldots+\frac{\rho^nT^n}{n!}\right] = G_0e^{\rho T}$$

&

Now $\lim_{n\to\infty} W_n(X,T) = W(X,T)$ & $\lim_{n\to\infty} G_n(X,T) = G(X,T)$.

$\therefore W(X,T) = W_0e^{\rho T}$ & $G(X,T) = G_0e^{\rho T}$

Numerical Parameters:

Parameters	**High ρ**	**Low ρ**
No. of Cells in White Matter	$W_0 = 40{,}000 \; cells/cm^2$ [9,10]	$W_0 = 40{,}000 \; cells/cm^2$
Growth Rate in White Matter	ρ_W 0.012 cm/day [9,10]	ρ_W 0.008 cm/day
No. of Cells in Gray Matter	$G_0 = 8000 \; cells/cm^2$	$G_0 = 8000 \; cells/cm^2$
Growth Rate in Gray Matter	ρ_G 0.012 cm/day [9,10]	ρ_G 0.008 cm/day [9,10]

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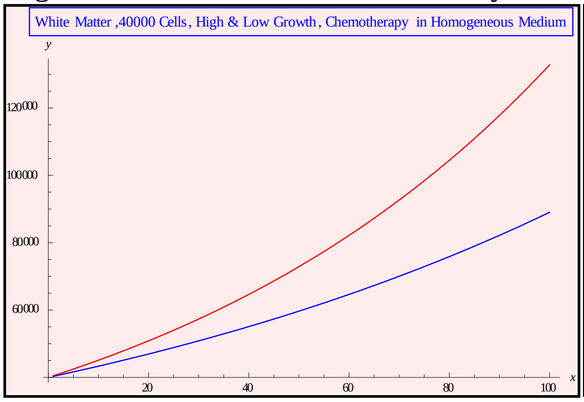
Graphical Representation:

High & Low ρ in White Matter &Gray matter



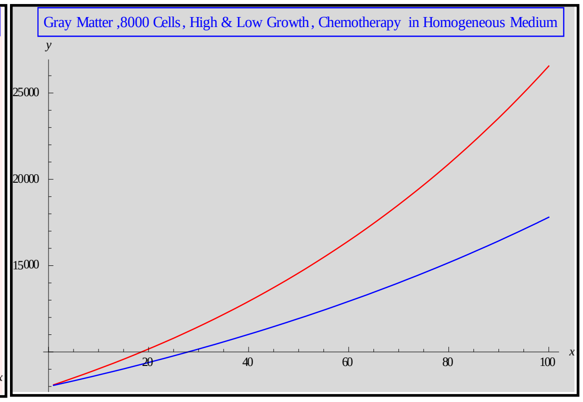


Fig.2 High & Low Growth in White Matter **Fig.3 High & Low Growth in Gray Matter**

Conclusion:

From the graph we can conclude that in White and Gray Matter both, no. of cells for high growth rate 3.375 times and for low growth rate 2.25 times than the original 40,000 no. of cells after 100 days.

Case:2When spread of early cancer cells are known:

Considering the appropriate form of the initial condition. Basically, tumor started with one cancerous cell. Initially the growth type and how much early cancer cells spread out are unknown. We can assume that at the time of the first scan, the process has already broken any previous uniform distribution of the cells. So, the cells are normally distributed with a maximum cell density $'a'$, and $'c'$, at the centre $'x_0'$ of the tumor in White and Gray matter respectively. [10]

i.e. $W(x,0) = a\,e^{-\frac{|x-x_0|^2}{b}}$ & $G(x,0) = c\,e^{-\frac{|x-x_0|^2}{d}}$; where b and d are the initial measurements of the tumor cells in white and gray matter respectively.

As we are considering Homogeneous Medium for one Dimensional GlioblastomaTumor cells growth, so either it occurs in White Matter or in Gray Matter, when spread of early cancer cells are known, defined as,

$$\frac{\partial W}{\partial t} = D\frac{\partial^2 W}{\partial x^2} + \rho W \; ; W(x,0) = a\,e^{-\frac{|x-x_0|^2}{b}} \qquad \text{(In White Matter) [9,10]} \qquad (7)$$

$$\frac{\partial G}{\partial t} = D\frac{\partial^2 G}{\partial x^2} + \rho G \; ; G(x,0) = c\,e^{-\frac{|x-x_0|^2}{d}} \qquad \text{(In Gray Matter) [9,10]} \qquad (8)$$

Using KVIM, we get the iterations as,

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$$W_1(x,t) = a\,e^{-\frac{|x-x_0|^2}{b}}\left\{1+\rho t-\frac{2Dt}{b}+\frac{4Dt|x-x_0|^2}{b^2}\right\}$$

$$W_2(x,t) = a\,e^{-\frac{|x-x_0|^2}{b}}\left\{\begin{array}{l}1+\rho t-\frac{2Dt}{b}+\frac{4Dt|x-x_0|^2}{b^2}-\frac{2D\rho t^2}{b}+\frac{6D^2t^2}{b^2}+\frac{\rho^2t^2}{2}\\+\frac{4\rho Dt^2|x-x_0|^2}{b^2}+\frac{8D^2t^2|x-x_0|^4}{b^4}-\frac{24D^2t^2|x-x_0|^2}{b^3}\end{array}\right\}\ \&$$

$\vdots$

$$G_1(x,t) = c\,e^{-\frac{|x-x_0|^2}{d}}\left\{1+\rho t-\frac{2Dt}{d}+\frac{4Dt|x-x_0|^2}{d^2}\right\}$$

$$G_2(x,t) = c\,e^{-\frac{|x-x_0|^2}{d}}\left\{\begin{array}{l}1+\rho t-\frac{2Dt}{d}+\frac{4Dt|x-x_0|^2}{d^2}-\frac{2D\rho t^2}{d}+\frac{6D^2t^2}{d^2}+\frac{\rho^2t^2}{2}\\+\frac{4\rho Dt^2|x-x_0|^2}{d^2}+\frac{8D^2t^2|x-x_0|^4}{d^4}-\frac{24D^2t^2|x-x_0|^2}{d^3}\end{array}\right\}\ \&$$

$\vdots$

Continuing in this manner and neglecting the higher order terms and $\lim_{n\to\infty} W_n(x,t) = W(x,t)$ and $\lim_{n\to\infty} G_n(x,t) = G(x,t)$. For calculation we used second iterations for both matters $W_2(x,t)$ & $G_2(x,t)$.

We calculate the values of High and Intermediate grade only, as Low grade tumors are not generally detectable in CT scan.

Numerical Parameters: For HH Grade (High ρ, High D)

Parameters	White Matter	Gray Matter
Velocity of Cells	$v_W = 0.018\ cm/day$ [9,10]	$v_G = 0.008\ cm/day$ [9,10]
Diffusion Rate	$D_W = 0.0065\ cm^2/day$ [9,10]	$D_G = 0.0013\ cm^2/day$ [9,10]
Growth Rate	$\rho_W = 0.012\ cm/day$ [9,10]	$\rho_G = 0.012\ cm/day$ [9,10]
Number of Cells	$W_0 = a = 40000$ & 500 [9,10]	$G_0 = c = 40000$ & 500 [9,10]
Measure of spread of tumor cells	$b = 0.8$ cm	$d = 0.4$ cm
Centre	$x_0 = 0$	$x_0 = 0$

Table:1 Case-2 HH Grade, White Matter, 40000 cells in Homogeneous Medium

t	x=0.1	x=0.2	x=0.3	x=0.4	x=0.5	x=0.6	x=0.7	x=0.8	x=0.9	x=1
0	39503.1	38049.2	35743.9	32749.2	29264.6	25505.1	21679.8	17973.2	14532.4	11460.2
10	39108.	37935.	36136.7	33731.9	30844.5	27978.7	24498.6	21208.3	18121.8	15092.9
20	40766.9	39418.8	37529.5	35042.6	32072.4	29788.3	26017.4	23005.4	20461.2	17739.6

30	44479.8	42500.6	39922.3	36681.3	32948.3	30933.9	26236.2	23364.5	21550.6	19400.3
40	50246.7	47180.4	43315.1	38648.	33472.2	31415.5	25155.	22285.6	21390.	20075.
50	58067.6	53458.2	47707.9	40942.7	33644.1	31233.1	22773.8	19768.7	19979.4	19763.7
60	67942.5	61334.	53100.7	43565.4	33464.	30386.7	19092.6	15813.8	17318.8	18466.4
70	79871.4	70807.8	59493.5	46516.1	32931.9	28876.3	14111.4	10420.9	13408.2	16183.1
80	93854.3	81879.6	66886.3	49794.8	32047.8	26701.9	7830.17	3589.96	8247.58	12913.8
90	109891.	94549.4	75279.1	53401.5	30811.7	23863.5	248.97	-4678.94	1836.98	8658.5
100	127982.	108817.	84671.9	57336.2	29223.6	20361.1	-8632.23	-14385.8	-5823.62	3417.2

Table: 2 Case-2 HH Grade, White Matter, 500 cells in Homogeneous Medium

t	**x=0.1**	**x=0.2**	**x=0.3**	**x=0.4**	**x=0.5**	**x=0.6**	**x=0.7**	**x=0.8**	**x=0.9**	**x=1**
0	493.79	475.61	446.8	409.37	365.81	318.81	270.99	224.66	181.65	143.25
10	488.99	474.21	451.5	421.57	385.51	349.81	306.29	265.06	226.35	188.85
20	510.19	492.81	468.2	437.77	400.81	372.61	325.39	287.46	255.05	222.45
30	557.39	531.41	496.9	457.97	411.71	387.21	328.29	291.86	267.75	244.05
40	630.59	590.01	537.6	482.17	418.21	393.61	314.99	278.26	264.45	253.65
50	729.79	668.61	590.3	510.37	420.31	391.81	285.49	246.66	245.15	251.25
60	854.99	767.21	655.	542.57	418.01	381.81	239.79	197.06	209.85	236.85
70	1006.19	885.81	731.7	578.77	411.31	363.61	177.89	129.46	158.55	210.45
80	1183.39	1024.41	820.4	618.97	400.21	337.21	99.79	43.86	91.25	172.05
90	1386.59	1183.01	921.1	663.17	384.71	302.61	5.49	-59.74	7.95	121.65
100	1615.79	1361.61	1033.8	711.37	364.81	259.81	-105.01	-181.34	-91.35	59.25

Table: 3 Case-2 HH Grade, Gray Matter, 40000 cells in Homogeneous Medium

t	**x=0.1**	**x=0.2**	**x=0.3**	**x=0.4**	**x=0.5**	**x=0.6**	**x=0.7**	**x=0.8**	**x=0.9**	**x=1**
0	39012.4	36193.5	31940.7	26812.8	21410.5	16262.8	11750.3	8075.86	5279.75	3283.4
10	41482.1	38824.7	34741.7	29845.2	24464.	19244.1	14411.4	10353.4	7085.25	4678.9
20	44365.8	41795.9	37778.7	33043.6	27629.5	22333.4	17224.5	12824.9	9122.75	6304.4
30	47663.5	45107.1	41051.7	36408.	30907.	25530.7	20189.6	15490.4	11392.3	8159.9
40	51375.2	48758.3	44560.7	39938.4	34296.5	28836.	23306.7	18349.9	13893.8	10245.4

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50	55500.9	52749.5	48305.7	43634.8	37798.	32249.3	26575.8	21403.4	16627.3	12560.9
60	60040.6	57080.7	52286.7	47497.2	41411.5	35770.6	29996.9	24650.9	19592.8	15106.4
70	64994.3	61751.9	56503.7	51525.6	45137.	39399.9	33570.	28092.4	22790.3	17881.9
80	70362.	66763.1	60956.7	55720.	48974.5	43137.2	37295.1	31727.9	26219.8	20887.4
90	76143.7	72114.3	65645.7	60080.4	52924.	46982.5	41172.2	35557.4	29881.3	24122.9
100	82339.4	77805.5	70570.7	64606.8	56985.5	50935.8	45201.3	39580.9	33774.8	27588.4

Table: 4 Case-2 HH Grade, Gray Matter, 500 cells in Homogeneous Medium

t	**x=0.1**	**x=0.2**	**x=0.3**	**x=0.4**	**x=0.5**	**x=0.6**	**x=0.7**	**x=0.8**	**x=0.9**	**x=1**
0	487.65	452.42	399.26	335.16	267.63	203.28	146.88	100.95	65.997	41.04
10	518.55	485.32	434.26	373.06	305.83	240.55	180.13	129.45	88.597	58.44
20	554.65	522.42	472.26	412.96	345.43	279.16	215.28	160.35	114.197	78.64
30	595.95	563.72	513.26	454.86	386.43	319.11	252.33	193.65	142.797	101.64
40	642.45	609.22	557.26	498.76	428.83	360.4	291.28	229.35	174.397	127.44
50	694.15	658.92	604.26	544.66	472.63	403.03	332.13	267.45	208.997	156.04
60	751.05	712.82	654.26	592.56	517.83	447.	374.88	307.95	246.597	187.44
70	813.15	770.92	707.26	642.46	564.43	492.31	419.53	350.85	287.197	221.64
80	880.45	833.22	763.26	694.36	612.43	538.96	466.08	396.15	330.797	258.64
90	952.95	899.72	822.26	748.26	661.83	586.95	514.53	443.85	377.397	298.44
100	1030.65	970.42	884.26	804.16	712.63	636.28	564.88	493.95	426.997	341.04

Graphical Representation: HH Grade: High ρ, High D

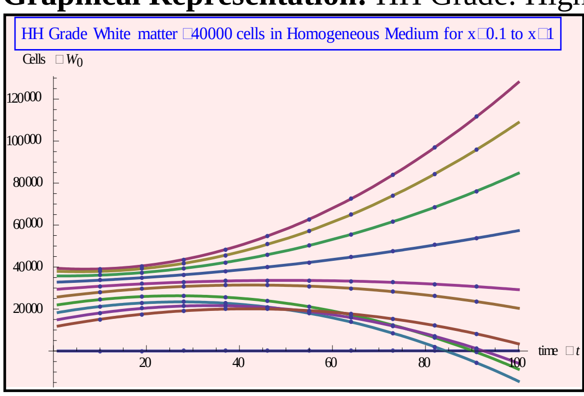

Fig. 4 HH Grade, White Matter, 40000 Cells

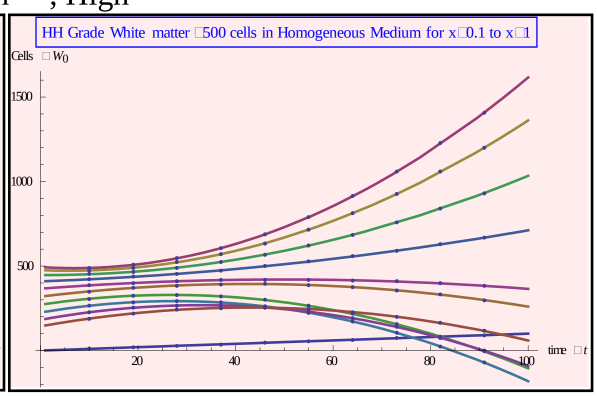

Fig. 5 HH Grade, White Matter, 500 Cells

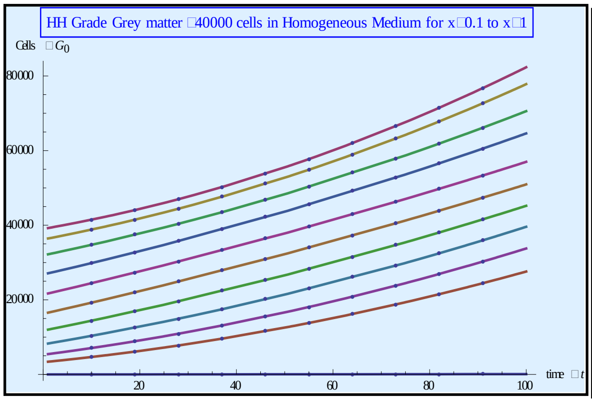

Fig. 6 HH Grade, Gray Matter, 40000 Cells

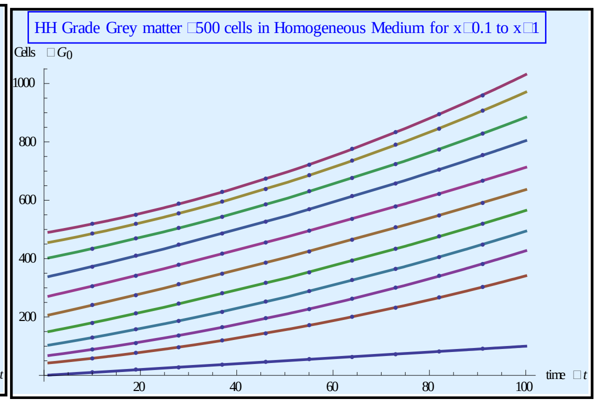

Fig. 7 HH Grade, Gray Matter, 500 Cells

Numerical Parameters: For HL Grade (High ρ, Low D)

Parameters	**White Matter**	**Gray Matter**
Velocity of Cells	$v_W = 0.00088\ cm/day$	$v_G = 0.0004\ cm/day$
Diffusion Rate	$D_W = 0.000016\ cm^2/day$	$D_G = 0.0000033\ cm^2/day$
Growth Rate	$\rho_W = 0.012\ cm/day$ [9,10]	$\rho_G = 0.012\ cm/day$ [9,10]
Number of Cells	$W_0 = a = 40000\ \&\ 500$ [9,10]	$G_0 = c = 40000\ \&\ 500$ [9,10]
Measure of spread of tumor cells	$b = 0.8$ cm	$d = 0.4$ cm
Centre	$x_0 = 0$	$x_0 = 0$

Table: 5 Case-2 HL Grade, White Matter, 40000 Cells in Homogeneous Medium

t	**x=0.1**	**x=0.2**	**x=0.3**	**x=0.4**	**x=0.5**	**x=0.6**	**x=0.7**	**x=0.8**	**x=0.9**	**x=1**
0	39503.1	38049.2	35743.9	32749.2	29264.6	25505.1	21679.8	17973.2	14532.4	11460.2
10	44527.5	42889.1	40290.2	36915.1	32987.4	28749.5	24437.4	20259.	16382.3	12919.4
20	50119.9	48277.	45350.5	41553.	37132.2	32361.9	27507.	22802.8	18444.2	14546.6
30	56280.3	54212.9	50924.8	46662.9	41699.	36342.3	30888.6	25604.6	20718.1	16341.8
40	63008.7	60696.8	57013.1	52244.8	46687.8	40690.7	34582.2	28664.4	23204.	18305.
50	70305.1	67728.7	63615.4	58298.7	52098.6	45407.1	38587.8	31982.2	25901.9	20436.2
60	78169.5	75308.6	70731.7	64824.6	57931.4	50491.5	42905.4	35558.	28811.8	22735.4
70	86601.9	83436.5	78362.	71822.5	64186.2	55943.9	47535.	39391.8	31933.7	25202.6
80	95602.3	92112.4	86506.3	79292.4	70863.	61764.3	52476.6	43483.6	35267.6	27837.8
90	105171.	101336.	95164.6	87234.3	77961.8	67952.7	57730.2	47833.4	38813.5	30641.

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100	115307.	111108.	104337.	95648.2	85482.6	74509.1	63295.8	52441.2	42571.4	33612.2

Table: 6 Case-2 HL Grade, White Matter, 500 Cells in Homogeneous Medium

t	**x=0.1**	**x=0.2**	**x=0.3**	**x=0.4**	**x=0.5**	**x=0.6**	**x=0.7**	**x=0.8**	**x=0.9**	**x=1**
0	493.79	475.61	446.8	409.37	365.81	318.81	270.99	224.66	181.65	143.25
10	556.69	536.11	503.6	461.37	412.31	359.41	305.49	253.26	204.75	161.45
20	626.79	603.41	566.8	519.17	464.01	404.61	343.99	285.06	230.45	181.65
30	704.09	677.51	636.4	582.77	520.91	454.41	386.49	320.06	258.75	203.85
40	788.59	758.41	712.4	652.17	583.01	508.81	432.99	358.26	289.65	228.05
50	880.29	846.11	794.8	727.37	650.31	567.81	483.49	399.66	323.15	254.25
60	979.19	940.61	883.6	808.37	722.81	631.41	537.99	444.26	359.25	282.45
70	1085.29	1041.91	978.8	895.17	800.51	699.61	596.49	492.06	397.95	312.65
80	1198.59	1150.01	1080.4	987.77	883.41	772.41	658.99	543.06	439.25	344.85
90	1319.09	1264.91	1188.4	1086.17	971.51	849.81	725.49	597.26	483.15	379.05
100	1446.79	1386.61	1302.8	1190.37	1064.81	931.81	795.99	654.66	529.65	415.25

Table: 7 Case-2 HL Grade, Gray Matter, 40000 Cells in Homogeneous Medium

t	**x=0.1**	**x=0.2**	**x=0.3**	**x=0.4**	**x=0.5**	**x=0.6**	**x=0.7**	**x=0.8**	**x=0.9**	**x=1**
0	39012.4	36193.5	31940.7	26812.8	21410.5	16262.8	11750.3	8075.86	5279.75	3283.4
10	43974.9	40797.7	36003.6	30223.3	24133.8	18331.3	13245.3	9102.96	5951.35	3701.4
20	49499.4	45923.9	40526.5	34019.8	27165.1	20633.8	14910.3	10246.1	6698.95	4167.4
30	55585.9	51572.1	45509.4	38202.3	30504.4	23170.3	16745.3	11505.2	7522.55	4681.4
40	62234.4	57742.3	50952.3	42770.8	34151.7	25940.8	18750.3	12880.3	8422.15	5243.4
50	69444.9	64434.5	56855.2	47725.3	38107.	28945.3	20925.3	14371.4	9397.75	5853.4
60	77217.4	71648.7	63218.1	53065.8	42370.3	32183.8	23270.3	15978.5	10449.4	6511.4
70	85551.9	79384.9	70041.	58792.3	46941.6	35656.3	25785.3	17701.6	11577.	7217.4

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80	94448.4	87643.1	77323.9	64904.8	51820.9	39362.8	28470.3	19540.7	12780.6	7971.4
90	103907.	96423.3	85066.8	71403.3	57008.2	43303.3	31325.3	21495.8	14060.2	8773.4
100	113927.	105726.	93269.7	78287.8	62503.5	47477.8	34350.3	23566.9	15415.8	9623.4

Table: 8 Case-2 HL Grade, Gray Matter, 500 Cells in Homogeneous Medium

t	x=0.1	x=0.2	x=0.3	x=0.4	x=0.5	x=0.6	x=0.7	x=0.8	x=0.9	x=1
0	487.65	452.42	399.26	335.16	267.63	203.28	146.88	100.95	65.997	41.04
10	549.65	510.02	450.06	377.76	301.63	229.18	165.58	113.78	74.367	46.24
20	618.65	574.22	506.66	425.16	339.43	258.08	186.48	128.07	83.677	52.04
30	694.65	645.02	569.06	477.36	381.03	289.98	209.58	143.82	93.927	58.44
40	777.65	722.42	637.26	534.36	426.43	324.88	234.88	161.03	105.117	65.44
50	867.65	806.42	711.26	596.16	475.63	362.78	262.38	179.7	117.247	73.04
60	964.65	897.02	791.06	662.76	528.63	403.68	292.08	199.83	130.317	81.24
70	1068.65	994.22	876.66	734.16	585.43	447.58	323.98	221.42	144.327	90.04
80	1179.65	1098.02	968.06	810.36	646.03	494.48	358.08	244.47	159.277	99.44
90	1297.65	1208.42	1065.26	891.36	710.43	544.38	394.38	268.98	175.167	109.44
100	1422.65	1325.42	1168.26	977.16	778.63	597.28	432.88	294.95	191.997	120.04

Graphical Representation: HL Grade: High ρ, Low D

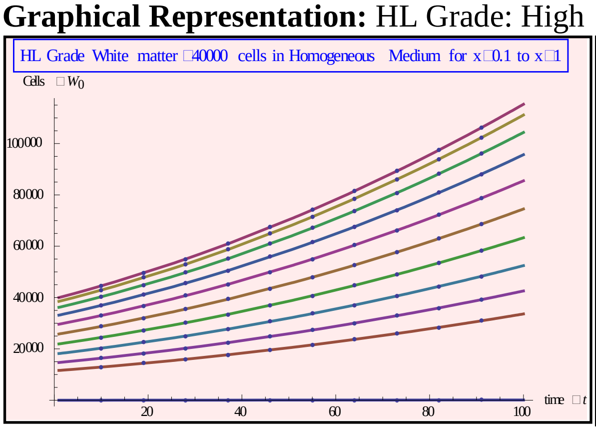

Fig. 8 HL Grade, White Matter, 40000 Cells

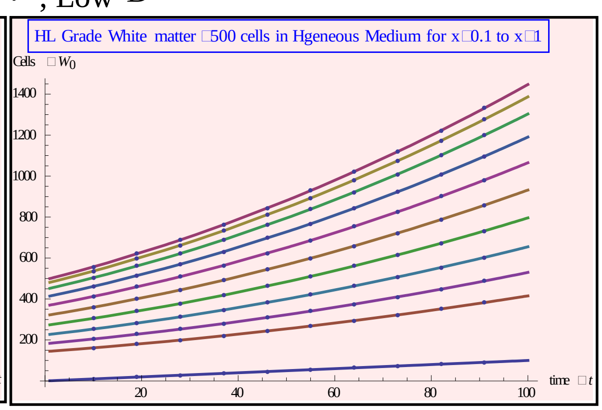

Fig. 9 HL Grade, White Matter, 500 Cells

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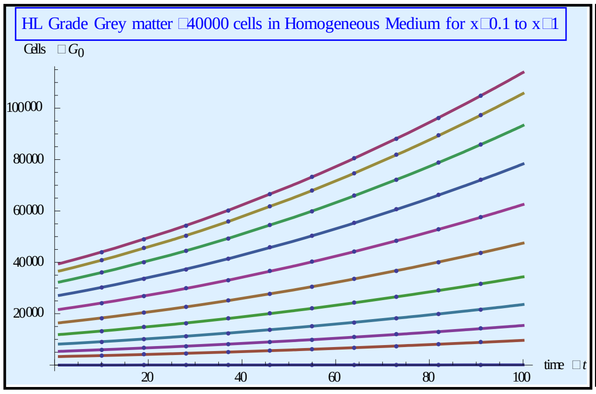

Fig. 10 HL Grade, Gray Matter, 40000 Cells

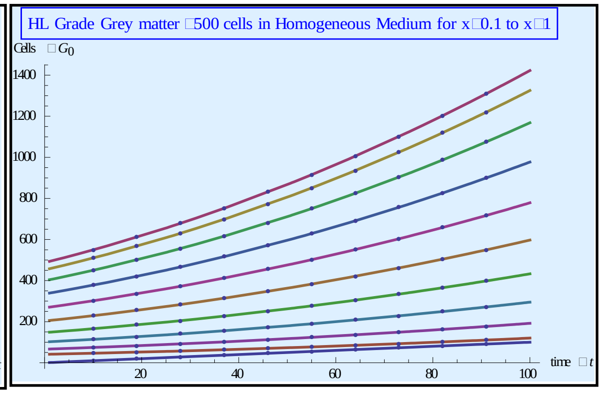

Fig. 11 HL Grade, Gray Matter, 500 Cells

Numerical Parameters: For LH Grade (Low ρ, High D)

Parameters	White Matter	Gray Matter
Velocity of Cells	$v_W = 0.018\ cm/day$	$v_G = 0.008\ cm/day$
Diffusion Rate	$D_W = 0.0065\ cm^2\ /\ day$	$D_G = 0.0013\ cm^2\ /\ day$
Growth Rate	$\rho_W = 0.008\ cm/day$	$\rho_G = 0.008\ cm/day$
Number of Cells	$W_0 = a = 40000$ & 500 [9,10]	$G_0 = c = 40000$ & 500 [9,10]
Measure of spread of tumor cells	$b = 0.8$ cm	$d = 0.4$ cm
Centre	$x_0 = 0$	$x_0 = 0$

Table: 9 Case-2 LH Grade, White Matter, 40000 Cells in Homogeneous Medium

t	x=0.1	x=0.2	x=0.3	x=0.4	x=0.5	x=0.6	x=0.7	x=0.8	x=0.9	x=1
0	39503.1	38049.2	35743.9	32749.2	29264.6	25505.1	21679.8	17973.2	14532.4	11460.2
10	37804.9	36679.1	34921.9	32559.3	29761.9	26984.4	23782.4	20453.4	17497.5	14485.5
20	38714.7	37439.	35529.9	32972.	30083.2	27851.5	24887.	21423.6	19126.6	16226.8
30	42232.5	40328.9	37567.9	33987.3	30228.5	28106.4	24993.6	20883.8	19419.7	16684.1
40	48358.3	45348.8	41035.9	35605.2	30197.8	27749.1	24102.2	18834.	18376.8	15857.4
50	57092.1	52498.7	45933.9	37825.7	29991.1	26779.6	22212.8	15274.2	15997.9	13746.7
60	68433.9	61778.6	52261.9	40648.8	29608.4	25197.9	19325.4	10204.4	12283.	10352.
70	82383.7	73188.5	60019.9	44074.5	29049.7	23004.	15440.	3624.56	7232.08	5673.3
80	98941.5	86728.4	69207.9	48102.8	28315.	20197.9	10556.6	-4465.24	845.18	-289.4
90	11810	10239	79825.	52733.	27404.	16779.	4675.1	-	-	-

	7.	8.	9	7	3	6	7	14065.	6877.72	7536.1
100	139881.	120198.	91873.9	57967.2	26317.6	12749.1	-2204.23	-25174.8	-15936.6	-16066.8

Table: 10 Case-2 LH Grade, White Matter, 500 Cells in Homogeneous Medium

t	**x=0.1**	**x=0.2**	**x=0.3**	**x=0.4**	**x=0.5**	**x=0.6**	**x=0.7**	**x=0.8**	**x=0.9**	**x=1**
0	493.79	475.61	446.8	409.37	365.81	318.81	270.99	224.66	181.65	143.25
10	472.29	458.21	436.6	407.27	372.01	337.11	297.49	256.06	219.05	181.05
20	482.79	466.81	444.4	413.17	376.01	347.41	311.99	269.46	240.45	202.85
30	525.29	501.41	470.2	427.07	377.81	349.71	314.49	264.86	245.85	208.65
40	599.79	562.01	514.	448.97	377.41	344.01	304.99	242.26	235.25	198.45
50	706.29	648.61	575.8	478.87	374.81	330.31	283.49	201.66	208.65	172.25
60	844.79	761.21	655.6	516.77	370.01	308.61	249.99	143.06	166.05	130.05
70	1015.29	899.81	753.4	562.67	363.01	278.91	204.49	66.46	107.45	71.85
80	1217.79	1064.41	869.2	616.57	353.81	241.21	146.99	-28.14	32.85	-2.35
90	1452.29	1255.01	1003.	678.47	342.41	195.51	77.49	-140.74	-57.75	-92.55
100	1718.79	1471.61	1154.8	748.37	328.81	141.81	-4.01	-271.34	-164.35	-198.75

Table: 11 Case-2 LH Grade, Gray Matter, 40000 Cells in Homogeneous Medium

t	**x=0.1**	**x=0.2**	**x=0.3**	**x=0.4**	**x=0.5**	**x=0.6**	**x=0.7**	**x=0.8**	**x=0.9**	**x=1**
0	39012.4	36193.5	31940.7	26812.8	21410.5	16262.8	11750.3	8075.86	5279.75	3283.4
10	39870.6	37311.9	33375.1	28606.6	23424.9	18498.6	13857.2	9952.26	6807.05	4498.6
20	41040.8	38640.3	34867.5	30395.	25357.3	20652.4	15947.7	11866.7	8432.35	5845.8
30	42523.0	40178.7	36417.9	32178.	27207.7	22724.2	18021.8	13819.1	10155.7	7325.
40	44317.2	41927.1	38026.3	33955.6	28976.1	24714.	20079.5	15809.5	11977.	8936.2
50	46423.4	43885.5	39692.7	35727.8	30662.5	26621.8	22120.8	17837.9	13896.3	10679.4
60	48841.6	46053.9	41417.1	37494.6	32266.9	28447.6	24145.7	19904.3	15913.6	12554.6
70	51571.8	48432.3	43199.5	39256.	33789.3	30191.4	26154.2	22008.7	18028.9	14561.8
80	54614.	51020.7	45039.9	41012.	35229.7	31853.2	28146.3	24151.1	20242.2	16701.
90	57968.2	53819.1	46938.3	42762.6	36588.1	33433.	30122.	26331.5	22553.5	18972.2
100	61634.4	56827.5	48894.7	44507.8	37864.5	34930.8	32081.3	28549.9	24962.8	21375.4

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Table:12 Case-2 LH Grade, Gray Matter, 500 Cells in Homogeneous Medium

t	x=0.1	x=0.2	x=0.3	x=0.4	x=0.5	x=0.6	x=0.7	x=0.8	x=0.9	x=1
0	487.65	452.42	399.26	335.16	267.63	203.28	146.88	100.95	65.997	41.04
10	498.35	466.42	417.22	357.694	292.82	231.27	173.18	124.38	85.107	56.26
20	512.85	483.02	435.9	380.296	316.99	258.24	199.28	148.27	105.437	73.12
30	531.15	502.22	455.3	402.966	340.14	284.19	225.18	172.62	126.987	91.62
40	553.25	524.02	475.42	425.704	362.27	309.12	250.88	197.43	149.757	111.76
50	579.15	548.42	496.26	448.51	383.38	333.03	276.38	222.7	173.747	133.54
60	608.85	575.42	517.82	471.384	403.47	355.92	301.68	248.43	198.957	156.96
70	642.35	605.02	540.1	494.326	422.54	377.79	326.78	274.62	225.387	182.02
80	679.65	637.22	563.1	517.336	440.59	398.64	351.68	301.27	253.037	208.72
90	720.75	672.02	586.82	540.414	457.62	418.47	376.38	328.38	281.907	237.06
100	765.65	709.42	611.26	563.56	473.63	437.28	400.88	355.95	311.997	267.04

Graphical Representation: LH Grade: Low ρ, High D

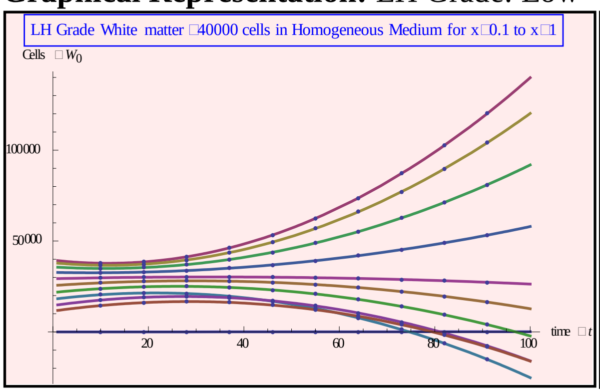

Fig. 12 LH Grade, White Matter, 40000 Cells

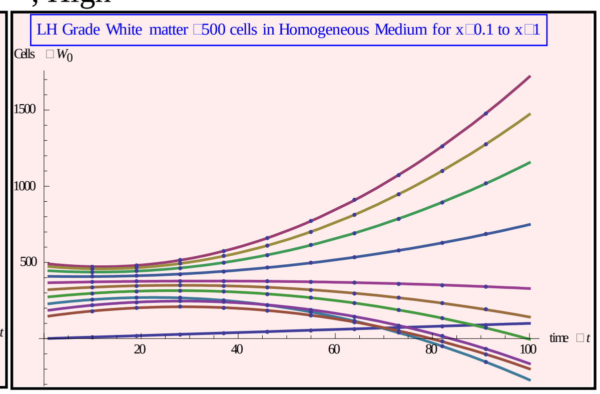

Fig. 13 LH Grade, White Matter, 500 Cells

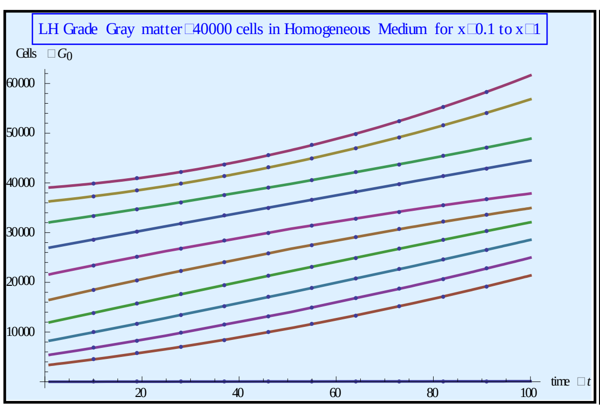

Fig. 14 LH Grade, Gray Matter, 40000 Cells

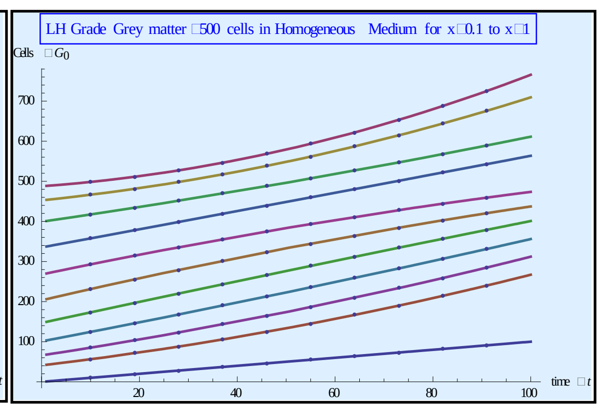

Fig. 15 LH Grade, Gray Matter, 500 Cells

Conclusion for Case-2

Grade	**White Matter-40000 Cells (After 100 Days-Tumor size)**	**White Matter-500 Cells (After 100 Days-Tumor size)**
HH	1,20,000 Cells, A=3 cm^2, r=0.98 cm, D=1.96 cm, Patient lives 330 days	1500 Cells, A=0.0375 cm^2, r=0.012 cm, D=0.024 cm, Patient lives 26395 days
HL	1,10,000 Cells, A=2.75 cm^2, r=0.88 cm,	1400 Cells, A=0.035 cm^2, r=0.11 cm,

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	D=1.76 cm, Patient lives 360 days	D=0.22 cm, Patient lives 28280 days
LH	1,40,000 Cells, A=3.5 cm^2, r=1.06 cm, D=2.12 cm, Patient lives minimum 283 days	1700 Cells, A=0.043 cm^2, r=0.12 cm, D=0.24 cm, Patient lives minimum 23290 days
Grade	**Gray Matter-40000 Cells (After 100 Days-Tumor size)**	**Gray Matter-500 Cells (After 100 Days-Tumor size)**
HH	80,000 Cells, A=2 cm^2, r=0.80 cm, D=1.60 cm, Patient lives 495 days	1000 Cells, A=0.025 cm^2, r=0.089 cm, D=0.178 cm, Patient lives 39592 days
HL	1,10,000 Cells, A=2.75 cm^2, r=0.88 cm, D=1.76 cm, Patient lives 360 days	1400 Cells, A=0.035 cm^2, r=0.11 cm, D=0.22 cm, Patient lives 28280 days
LH	60,000 Cells, A=1.5 cm^2, r=0.69 cm, D=1.38 cm, Patient lives minimum 660 days	800 Cells, A=0.02 cm^2, r=0.08 cm, D=0.16 cm, Patient lives minimum 49490 days

Patient: 01 (Bharat Cancer Hospital, Surat, Gujarat, India)

Name: DevyaniChauhan**Age:** 22 Years **Date of Report Execute: 20-01-2020**

Size: approximately $17 \times 23 \times 21\ mm \quad i.e.\ 1.7 \times 2.3 \times 2.1\ cm$

No. of Cells: $[22666\ ,\ 30666\ ,\ 28000]$. So, average is 27110 cells in detected tumor.

She has Low Grade Glioma in Homogeneous Medium.

Numerical Parameters:

Parameters	**White Matter**	**Gray Matter**
Velocity of Cells	$v_W = 0.018\ cm/day$	$v_G = 0.008\ cm/day$
Diffusion Rate	$D_W = 0.0065\ cm^2\ /\ day$	$D_G = 0.0013\ cm^2\ /\ day$
Growth Rate	$\rho_W = 0.008\ cm/day$	$\rho_G = 0.008\ cm/day$
Number of Cells	$W_0 = a = 27110$	$G_0 = c = 27110$
Measure of spread of tumor cells	$b = 0.8$	$d = 0.4$
Centre	$x_0 = 0$	$x_0 = 0$

Table:13 LH Grade, White Matter, 27110 Cells in Homogeneous Medium

t	**x=0.1**	**x=0.2**	**x=0.3**	**x=0.4**	**x=0.5**	**x=0.6**	**x=0.7**	**x=0.8**	**x=0.9**	**x=1**
0	26773.2	25787.8	24225.4	22195.8	19834.1	17286.1	14693.5	12181.3	9849.32	7767.15
10	25622.4	24859.4	23668.7	22066.9	20170.8	18289.1	16118.7	13861.9	11858.6	9817.65
20	26239.6	25375.	24082.	22346.	20387.5	18878.1	16867.9	14518.5	12961.9	10998.2
30	28624.8	27334.6	25465.3	23033.1	20484.2	19053.1	16941.1	14151.1	13159.2	11308.7
40	32778.	30738.2	27818.6	24128.2	20460.9	18814.1	16338.3	12759.7	12450.5	10749.2
50	38699.2	35585.8	31141.9	25631.3	20317.6	18161.1	15059.5	10344.3	10835.8	9319.65

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60	46388.4	41877.4	35435.2	27542.4	20054.3	17094.1	13104.7	6904.91	8315.12	7020.15
70	55845.6	49613.	40698.5	29861.5	19671.	15613.1	10473.9	2441.51	4888.42	3850.65
80	67070.8	58792.6	46931.8	32588.6	19167.7	13718.1	7167.06	-3045.89	555.72	-188.85
90	80064.	69416.2	54135.1	35723.7	18544.4	11409.1	3184.26	-9557.29	-4682.98	-5098.35
100	94825.2	81483.8	62308.4	39266.8	17801.1	8686.1	-1474.54	-17092.7	-10827.7	-10877.8

Graphical Representation: LH Grade, White Matter, 27110 cells in Homogeneous Medium

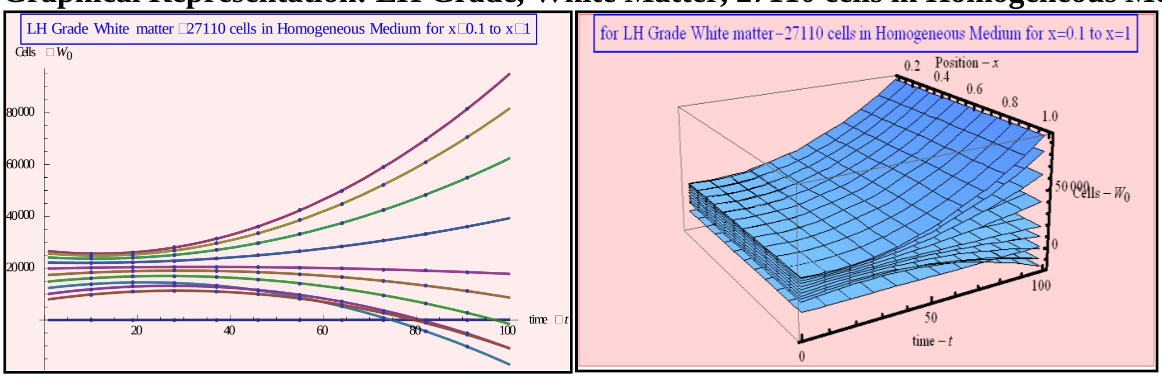

Fig. 16 Patient-1 LH Grade, White Matter, 27110 Cells – in 2D & 3D

Table: 14 LH Grade, Gray Matter, 27110 Cells in Homogeneous Medium

t	x=0.1	x=0.2	x=0.3	x=0.4	x=0.5	x=0.6	x=0.7	x=0.8	x=0.9	x=1
0	26440.7	24530.1	21647.8	18172.4	14510.9	11022.1	7963.77	5473.41	3578.35	2225.32
10	27022.6	25287.9	22620.3	19387.9	15875.	12537.6	9391.27	6745.31	4613.25	3049.22
20	27816.5	26187.7	23632.8	20599.4	17181.1	13997.9	10806.8	8043.21	5714.15	3963.12
30	28822.4	27229.5	24685.3	21806.9	18429.2	15403.	12210.3	9367.11	6881.05	4967.02
40	30040.3	28413.3	25777.8	23010.4	19619.3	16752.9	13601.8	10717.	8113.95	6060.92
50	31470.2	29739.1	26910.3	24209.9	20751.4	18047.6	14981.3	12092.9	9412.85	7244.82
60	33112.1	31206.9	28082.8	25405.4	21825.5	19287.1	16348.8	13494.8	10777.8	8518.72
70	34966.	32816.7	29295.3	26596.9	22841.6	20471.4	17704.3	14922.7	12208.7	9882.62
80	37031.9	34568.5	30547.8	27784.4	23799.7	21600.5	19047.8	16376.6	13705.6	11336.5

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90	39309.8	36462.3	31840.3	28967.9	24699.8	22674.4	20379.3	17856.5	15268.5	12880.4
100	41799.7	38498.1	33172.8	30147.4	25541.9	23693.1	21698.8	19362.4	16897.4	14514.3

Graphical Representation: LH Grade, Gray Matter, 27110 cells in Homogeneous Medium

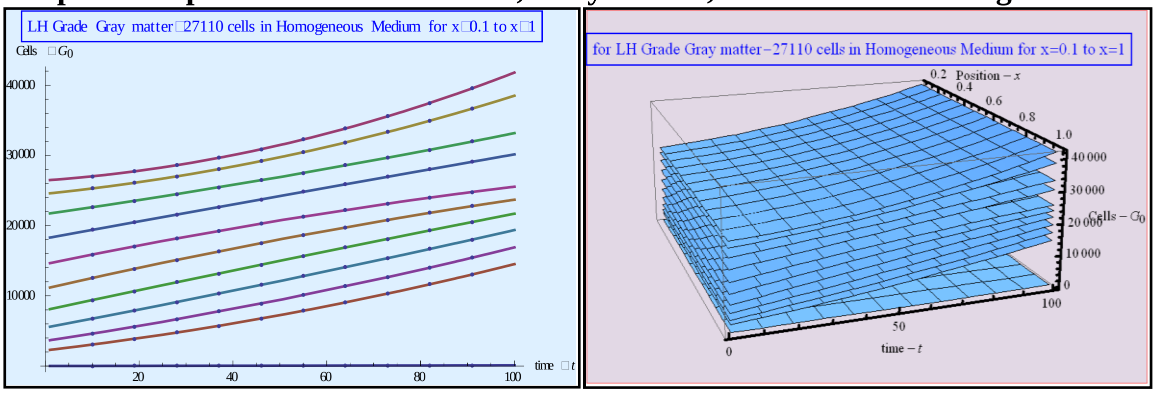

Fig. 17 Patient-1 LH Grade, Gray Matter, 27110 Cells in 2D & 3D

Conclusion:

Grade	**White Matter-27110 Cells (After 100 Days-Tumor size)**	**Gray Matter-27110 Cells (After 100 Days-Tumor size)**
LH	90,000 Cells, A=2.25 cm^2, r=0.85 cm, D=1.70 cm, Patient lives minimum 440 days	40,000 Cells, A=1 cm^2, r=0.56 cm, D=1.12 cm, Patient lives minimum 990 days

Conclusion:

Kamal Variational Iteration Method has been used to solve the mathematical models of Glioblastomatumor cells growth in White and Grey matter for High grade and Intermediate grade.

Advantage of using transformation upon variational Iteration method, it will become easy to find Lagrange Multiplier, as using Variational iteration method for higher order it is tangible to find it. Here I have applied New Integral Transform-Kamal Transform upon VIM. Sometimes it makes joyful and for getting satisfaction by doing some different and new things for getting the solution by applying the new arrival of transform upon VIM. Here both possessions are fully satisfied with getting good approximations results which highly matches with the given data.

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