Mathematical Approximation of Glioblastoma Disease

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Abstract— *the cures of some of mental and physical diseases are either less or nearly zero. Countable symptoms for mental diseases are not showing on early stage. So those treatments of mental diseases are comparatively less than the physical diseases. Nevertheless, some of physical diseases are also under in severe condition. Glioblastoma (GBM) is one of them. It generates from unbalancing of astrocytes. Critical condition in Glioblastoma is those types of tumors are increases rapidly and they are cozy in enormous structure of blood vessels. Cerebellum Hemisphere is most common effected area for Glioblastoma. It also covers Tentorium, Tectum and Fourth ventricle. Longer Stress, drug addiction depression are the source for producing it. Mathematically Continuum tumor growth model that defined output of Glioblastoma. Micro-environmental components described by continuum and the behavior of cell defined by discrete value of some mathematical equations like Darcy and long rage survival equations.*

Keywords- Glioblastoma; Types and Symptoms; Mathematical Stage; Approximate result

I. GLIOBLASTOMA GENERATION

Glioblastoma is defining by infected cell transfer infection rapidly with shorter period. It is rare identify in its primary stage (Increase without a known antecedent). Moreover, treatment of its higher stage is difficult and survival rate tens to zero. If compare this disease with rare treated disease like cancer, both having same range in terms of survival process. The development rate of glioma will give traumatic brain injury, retinoblastoma, Turcot syndrome, tuberous sclerosis, Li-Fraumeni syndrome and more. Another problem is medical science still try to find its perfect medicine. They have found the core part of Glioblastomas is genomic understanding. [1]

As per World Health Organization (WHO) [Report published in 2014 and 2007], glioblastoma is initial abnormal augmentation of tissue in brain. It encompasses 15% of initial abnormal augmentation of tissue and 60-75% of glial cells (cells which are basically work under central nervous system) and this type of tumor generally effect on inner side of brain : up to cerebrum. GBM represent Glioblastoma Multiform but as per WHO now multiform having no longer use. WHO also define a category of astrocytoma where Glioblastoma secure 4^{th} grade, in which gliomas represented with high-grade infection? In addition, in this stage treatment is probably by chemotherapy or by radiation. [1]

Generally, the presence of GBM is nearly 50's but it also present in teen age. Male and Female ratio of generation of this tumor is approximated 1.6:1.

Treatment with drug is Temozolomide (Temodal brand) where radiation is also a part of process. Complete surgical analysis of GBM is complicated because of its swift increment and possession of remaining brain area. Brain area which controls voice, thinking, visualization, memory storage and more [4]

Chemoradiation is one of the treatments in which patient waits for four weeks for the craniotomy. In Radiation Therapy it takes with TMZ also this both in parallel treatment give more benefit then RT alone. As per tumor article data of America (Sep. 2009): variance between RT+TMZ vs TMZ is 20.66% more survival. RT and TMZ use methylation process (Methane's alkyl form are added to the DNA particle) for finding Multiform Glioblastoma. In simple meaning, this process repairs the DNA cells which are deactivated. RT find DNA damage and its position then trigger the toxic cells which are infected /Dead or inactive. [5] But side effects of RT+TMZ are nausea, myelosuppression, constipation and fatigue while treatment in final stage and in early stage dysgeusia, alopecia, anorexia. [6], [7] and [8]

Betterment in treatment will achieve more efficiency and give life with quality. Current treatments like MRI and DTI (Diffusion Tensor Imaging), ultrasound surgery acceptable for triangulation multi-model that represents specific smaller and larger data of patient's anatomy. Another effective area is the use of 5 ALA that is aminolevulinic acid. Still in current years, those technologies are not sufficient. Other limitations are cost and the specific equipments and specialized surgeons. A standard of proper medicine with amount is also in way. [4]

II. MATHEMATICAL RESPONSE OF GLIOBLASTOMA

The model defines two types of cells:

1. Inactive Cells

2. Active Cells.

Inactive Cells production is 1:2 cell generation with the symmetric ratio "Ri" where both cells are in survive stage. In same manner asymmetric rate "Ra" for producing one active and one inactive cell with the ratio of 1:1 and 1: x respectively. If active and inactive cell reproduction combination is asymmetric then chances of tumor are more. If inactive cells are more and not converted into the active cells then after certain period some part of brain will infected by inactive cells this is nothing but tumor. In this process, if inactive cells are retrieves with active stage with rate of "v" and active cells are active with rate of "y". [10]

If both the cells pass through RT, inactive cells are radio resistive and active cells are reactive basis on the radiation and give response. Generation and death process of cells are linear then it is represented by quadratic function of survival cells Rate:

Survival Rate: Exp $[-(\alpha d+\beta d^2)]$ … (Author 1)

Where, α=Cell killing form as a result with single radiation,

β=Cell killing form as a result with two radiation

α s= Will give the rate of active cells after single radiation. Those are healthy cells. βs= Will give the rate of inactive cells after single radiation. Those are infant active cells.

If inactive cell parameter is μ ($0\leq \mu\leq 1$) then survival cells are nothing but $\beta s = (1- \mu)\beta i$ and $\alpha s = (1- \mu)\alpha i$, Where αi and βi are inactive cells.

After radiation if inactive cells are converted into the active cells then the number of this conversion is assumed as K and rate is approximate "Rc". But for this assumption what are the initial amount of no of inactive and no of active cells need to define. If initial no of active and inactive cells are N_0 then, [10]

According to rate:

1. Survival Rate: $N_0(s)$* Exp $[-(\alpha sd+\beta sd^2)]$… (2)

2. Inactive Rate: N_0 (i)* Exp $[-(\alpha id+\beta id^2)]$… (3)

Final Value of no of increasing inactive cells after "t" time is:

$N_1(i)$= Initial no of inactive cells*converter cells from inactive to active cells+ Active cells*infected Active cells after "t" Times.

$$N_1(i) = [N_0(i) * e^{-(\alpha(i)d+\beta(i)d^2)}] * [\int_0^t (1-\mu K) * e^{-(\alpha(s)d_i+\beta(s)d_i^2)} d_i]$$

+

$$[[N_0(s) * e^{-(\alpha(s)d+\beta(s)d^2)}] * [\int_0^t (1-\mu) * e^{-(\alpha(i)d_s+\beta(i)d_s^2} d_s]]$$

… (4) (Author 1)

Apply Darcy's like law for inactive cells to active cells moment:

$$N_t(s) = -(\nabla(\mu) - \frac{\partial E}{\partial Rc_t} * \nabla Rc_t) \quad \text{… (5)}$$

$N_t(s)$ = Survival rate after T time

Partial derivation of energy of inactive cells to recovery rate that define, at which rate survival procedure is:

∇Rc_t = The growth of tumor in every axis

By equation 5,

The growths of inactive cells are more compare to active cells as a result cerebrum is more infected by tumor and hard to recover. Let consider "T" time is for operation then identify tumor's initial stage and if it is less infected then exactly at which time is the ending time of operation? That needs calculation. Means after that T time, there is no meaning of operation.

So, Long range survival equation is:

$$\frac{\partial Rc}{\partial T} + [\nabla \bullet \mu Rc] = \alpha_s \Delta Rc + \beta_s \mu Rc \quad \text{… (6)}$$

$\frac{\partial Rc}{\partial T}$ = Largest time to recover inactive cells to active cells where inactive cell recovery is higher than infected cells.

RESULT

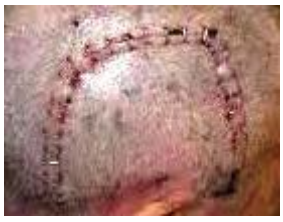

Fig. 1: The person who is suffering from Glioblastoma [9]

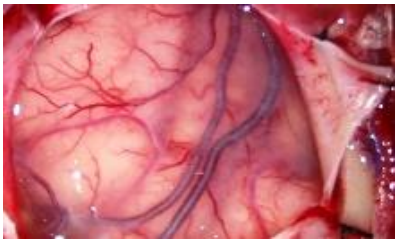

Fig. 2: Glioblastoma Formation [9]

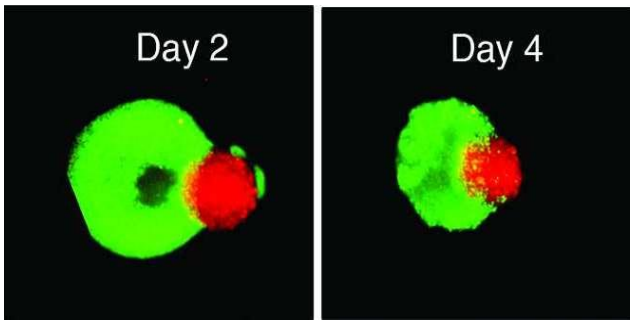

Fig. 3: Rapidly increasing movement of Glioblastoma [9]

CONCLUSION

This paper describe, by mathematical analysis and derivation Glioblastoma has identified and solve at any of the stage. It also describes the location of brain where the tumor is with 3D analysis. $N_t(s)$ give the result about is brain more infected or less infected by tumor. And what are the chances of survival of human before and after operation.

REFERENCES

[1] R.M. Young, A. Jamshidi, G.Davis and J.H.Sherman, "Current trends in the surgical management and treatment of adult glioblastoma", NCBI-June 2015, PP: 121

[2] H. Yan, M. Lopez, and others, "3D mathematical modeling of glioblastoma suggests that transdifferentiated vascular endothelial cells mediate resistance to current standard-of-care therapy",AACR-May 29, 2017

[3] M. Elizabeth Davis, "Glioblastoma: Overview of Disease and Treatment," HSS Public Access-Nov 25, 2016, PP: 1-8.

[4] Kuhnt D, Becker A, Ganslandt O, Bauer M, Buchfelder M, Nimsky C. "Correlation of the extent of tumor volume resection and patient survival in surgery of glioblastoma multiforme with high-field intraoperative MRI guidance", Neuro-Oncology, 2011; 13:1339–1348.

[5] Stupp R, Wong ET, Kanner AA, Steinberg D, Engelhard H, Heidecke V, Gutin PH. "NovoTTF-100A versus physician's choice chemotherapy in recurrent glioblastoma: A randomized phase III trial of a novel treatment modality". European Journal of Cancer. 2012; 48:2192–2202

[6] https://www.abta.org/tumor_types/glioblastoma-gbm/

[7] Schiff D, Lee EQ, Nayak L, Norden AD, Reardon DA, Wen P. "Medical management of brain tumors and the sequelae of treatment". Neuro-Oncology. 2015; 17:488–504.

[8] Niyazi M, Harter PN, Hattingen E, Rottler M, von Baumgarten L, Proescholdt M, Mittelbronn M., "Bevacizumab andRadiotherapy for the treatment of glioblastoma: Brothers in arms or unholy alliance?" Oncotarget. 2016; 7:2313–2328

[9] Google Images

[10] K. Leder, K.litter and Q. Laplant"Mathematical Modeling of PDGF-PDGF-Driven Glioblastoma Reveals Optimized Radiation Dosing Schedules", Elsevier-Jan 30 2014, PP: 603-616.

[11] Lee Y, Lee JK, Ahn SH, Lee J, Nam DH, "WNT signaling in glioblastoma and therapeutic opportunities". Lab Invest 2016; 96:137-50

[12] Frieboes HB, Jin F, Chuang YL, Wise SM, Lowengrub JS, Cristini V. Three-dimensional multispecies nonlinear tumor growth-II: Tumor invasion and angiogenesis. J Theor Biol 2010;264:1254-78