Oncology
and Radiotherapy ©
1 (52) 2020: 112-114 • Mini Review

Mathematical detection and successful management of gliomas

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SUMMARY

Inability of clinical oncologists to detect tumour early enough is a dreadful setback in management of gliomas. In view of this literatures were assessed for possible combination of mathematical parameters with scanning methods with intent to identifying all stages of gliomas that could be attacked inorder to slow down glioma growth invariably leading to increased life span. Findings have shown that gliomas of the volume of upto 20 cm^3 and 6 cm long could be removed surgically or arrested chemotherapeutically, but if left untreated for 1-7.2 years can kill. Hence consideration of glioma dimension is the key to successful management.

Key words: cancer, glioma, mathematics, management, prognosis, detection

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Word count: 2060 **Tables:** 00 **Figures:** 00 **References:** 32

Received: - 04 June, 2020

Accepted: - 15 June, 2020

Published: - 25 June, 2019

INTRODUCTION

Gliomas are fast-growing brain tumors that respond to early chemotherapy. However, ability to detect gliomas requires sophisticated scanning methods. The formula for sphere can be applied to estimate tumor volume, migration and proliferation. Glioma growth of 1-7.2 years if left untreated can kill, especially the gliomas of white matter. The rise of mathematical analogy could contribute to addressing the current challenges of understanding tumorigenesis and oncogenesis [1]. But over-optimistic estimations about its ability have created unrealistic expectations [2]. Cancer cells become visible and dangerous at few millimetres and centimetres becoming macroscopic with 10^8-10^{12} cells [3]. Brain metastases constitute less than 3% of primary tumors and intracranial neoplasm is common in adults but less common in children and very difficult to treat [4]. Also, 5%-10% of low-grade glioma has been reported which could be treated by excision and part resection with good prognosis and improvement of quality of life [5].

Mathematical Detection of Gliomas"

The proliferation-invasion model of glioma growth is presented mathematically using a partial differential equation [6] with two parameters: net rate of migration (D, mm^2/year) and proliferation (P, $year^{-2}$).

Rate of change of tumor cell density per time

$$= \frac{dC}{dt} \quad \text{(i)}$$

But the rate of change equals net migration of tumor cells+net proliferation of tumor cells in turn equals:

$$D(x) \times C + Pc\left(^{(1-/\frac{c}{K})}\right) \quad \text{(ii)}$$

Malignant glioma cells can migrate up to 100-fold faster in white matter than in gray matter, characterizing the extract of invisible subclinical disease. Therefore, the velocity of radial growth is mathematically presented as follows:

$$V = \sqrt{4Dp} \quad \text{(iii)}$$

But invisibility index = D/p (iv)

Equation ii provides Proliferation-Invasion Model (PI) of glioma growth and infiltration is similar to Fisher's equation similar with linear radial growth, seen in high and low-grade gliomas [7].

The growth of tumor relates sphere hence the total volume is equal to:

$$\frac{4}{3}\pi r^3 \quad \text{(v)}$$

Computational oncology has been applied to tumorigenesis passing through mutation to metastasis [8]. Hence stem cells (S) have unlimited reproductive potential as differentiated cells (D) which eventually die. Therefore:

$$S = (2p\,(D) - 1)\,v\,(D)\,S \quad \text{(vi)}$$

$$\text{Whereas } D = 2\,(1 - p\,(D))\,v\,(V)\,S - dD \quad \text{(vii)}$$

v=rate of division of stem cells; p=probability; d=rate of death; v (D)=rate of cell division; p (D)=probability of self-renewal [9].

Glioma growth of greater than 20 cm^3 has fewer prognoses with a short life span of the affected individuals. Therefore:

$$\text{Volume (V)} = \frac{4}{3}\pi r^3 \quad (\pi = 3.14159)$$

$$20\ cm^3 = \frac{4}{3} \times 3.14159 \times r^3$$

$$20\ cm^3 = 1.333 \times 3.14159 \times r^3$$

$$r^3 = \frac{20}{4.18773947} = 4.7758$$

$$r = \sqrt[3]{4.7758} = 1.68 \simeq 1.7cm$$

If radius of 1.7 cm is achieved, the movement translates to (1.7 × 10 mm)=17 mm. However the diameter becomes 17 mm × 2=34 mm=3.4 cm.

Management of Gliomas

Tumor growth of 1 cm= lg tumor =10^9 cancer cells, therefore 3.4 cm translate to 3.4 × 10^9=3.4 g of tumor weight. The estimation of 34 mm agrees with the report indicating that 5.8 mm per 1 year velocity was spontaneous and after 86.5 months (7.2 years) the velocity would have been 41.8 mm, when many affected patients would have died [10]. The model has provided insight into clinical behaviours such as survival outcome [11] and biological aggressiveness [12]. The final tumors of glioma in mice are 12 mm^3 to 62 mm^3 [13]. Cell degradation of glioma is 0.005/day with a steady tumor diameter between 0.1-10/day and cell migration velocity (6.5 μm/hr), tumor expansion (2.9 μm/hr) and tumor diameter (3 cm-6 cm) over 7 months [14]. The sphere formula can be used to estimate the volume of glioma cells, rate of growth and glioma cells population. Also, life expectancy can be determined using the formula. However, maximal migration distance can be predicted, but the migration of the main glioma cells can be underestimated [15]. Antineoplastic and end of life care is of topmost priority [16]. The survival rate of glioblastoma is 5 years [17] lower than that of glioma. It is diagnosed at the age of 45-70 years [18] treated by resection, radiotherapy and temozolomide [19]. Brain tumors are the second most common cause of cancer-related death in people of up to 35 years whose survival is still in months. About half of brain tumors are primary [20]. Weight of brain can be calculated using formula for Encephalization Quotient (EQ)= $\frac{E}{0.14} \times BW^{0.528}$, E=brain mass. E=kpβ, whereas p=body weight; k=constant; β=exponent (0.528). Hence, high EQ may denote low dose of anticancer for brain cancers such as gliomas [21]. Duration of glioblastoma cell line is 22-75 day with cell loss factor of 0.04-0.75, and sensitive radiation ray of 0.031-0.61 Gy and growth factor of 4%-46%, respectively [22] indicating that glioma growth rate (0.8-2.6%) is lower than that of embryonal tumor, malignant lymphoma, mesenchymal sarcoma, squamous cell carcinoma and adenocarcinoma [23]. Patients diagnosed of glioblastoma multiform could die within 2 years of treatment using temozolomide whose metabolite, methyl triazine imidazole carboxamide forms complex with alkyl guanine transferase [24]. Prognosis of high-grade glioma is poor with glioblastoma. Hence, there may be need to combine chemotherapy with radiotherapy [25]. High level of invasiveness of glioma is a big limitation to surgery and the tumor relapses in 80 % of cases within the range of 2 cm-3 cm of the margin of the original lesion [26]. The lesion of low grade glioma could be as high as ≥ 6 cm [27]. Patients with residual tumor volume of ≥ 15 cm^3 have benefit of survival [28] as against low-grade glioma of 5 cm [29].

Conclusion

Mathematics could be used to determine efficient delivery of free and nanoparticle-loaded delphinidin [30], clinical outcome, increase understanding of complex and random tumor behavior [31]. A multi scale mathematical theory is required to provide the appropriate frame work for developing reliable predictive mechanical models for oncogenesis and oncotherapy [2], knowledge of glymphatic system that takes into account basic cerebrovascular physiology and fluid transport may be of significance in oncotherapy [32]. Since growth rate of glioma and glioblastoma is much lower than those of other solid tumors, the two brain cancers could be managed better than some other solid tumors.

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