Advances and Applications in Mathematical Sciences
Volume 21, Issue 1, November 2021, Pages 447-458

APPROACH OF BOX COUNTING DIMENSION AND MATHEMATICAL MODELS OF LIVER CANCER

G. JAGAN KUMAR[1], G. JAYALALITHA[2] and M. RAVITHAMMAL[3]

[1]Research Scholar
[2]Professor
Department of Mathematics
VELS Institute of Science,
Technology and Advanced Studies
Chennai-600117, Tamil Nadu, India
E-mail: ultimategj1990@gmail.com
g.jayalalithamaths.sbs@velsuniv.ac.in

[3]Assistant Professor
Department of Mathematics
The Quaide Milleth College for Men
(Affiliated to University of Madras)
Chennai-600100, Tamil Nadu, India
E-mail:ravith_vahab1@yahoo.co.in

Abstract

Cancer is the one of the world most deadly diseases. This paper discusses the liver cancer cell development of tissue. The variety of surface unpredictability of cancer cell pictures are determined by Fractal dimension methods. Using the method of Box counting dimension, the fractal dimension of cancer cell images of growth pattern was calculated. Mathematical modelling to reproduce the growth rate of the cancer cells have been from Gompertz growth model. The statistical model explains the consistent growth of dimension of cancer cell. On observing the development of the cancer cell growth the pathologist can decide the evolution of the disease which assist with diagnosing the liver cancer and suggest suitable treatment.

2020 Mathematics Subject Classification: 81Q35, 81Q35, 62Qxx.

Keywords: Fractals, Box-counting dimension, Gompertz model, Cancer, Liver Cancer cell, Statistical analysis.

Received May 17, 2021; Accepted June 7, 2021

1. Introduction

1.1. Fractal

A fractal is a shape consisting of pieces that are identical in any way to the whole to view self-similarity properties, fractal object and process are described above [2]. A fractal is a structure that looks self-similar in various magnifying degrees. The major characteristics of fractal objects are self-similar. Recent studies have attempted to describe some parts of the body using fractal geometry, with some success [1]. An example of a fractal is the irregular shape of cancer cells.

2.2. Mathematical Model

Mathematical model is the utilization of arithmetic to depict true issue. Mathematical model in biology and medicine, the uses of numerical methods for getting valuable conclusion from the model and understanding complex organic medical circumstance [5]. It has created to comprehend the dynamical procedure of Cancer cell growth. It helps to foresee the cancer cell measure and streamline the treatment technique [6]. Mathematical models are used to better explain and treat cancer in a variety of ways. Models are used to explain the production and growth of cancer. A model of tumor growth is the base of every statistical model used to study cancer treatment.

1.3. Cancer Cell

Cancer growth is one of the world deadliest ailments, second driving reason for death on the world. Roughly 9.6 million deaths, around 1 out of 6 deaths is a result of cancer in 2018. Cancer is ordinarily started by hereditary changes that lead to improve the unusual of multiplication rate and cell development [4].

The abnormal growth of cells in the liver is known as liver cancer. Hepatocellular carcinoma is the most common form of liver cancer and it starts in cells called hepatocytes and its shows in figure 1. Cholangiocarcinoma and angiosarcoma are two less common types. The irregular changes in the DNA of liver cells cause liver cancer. Damage to the liver or infection may cause this. It can also happen at any time.

Anne Talkington, Rick Durrett, Estimating Tumor Growth Rates in different population growth models [11]. R. B. Ogunrinde and S. O. Ayinde demonstrate that the Gompertz cell growth models tumor growth accurately [12]. Calculating cell images using fractal dimension and models is given in section II. In section III the results are explained.

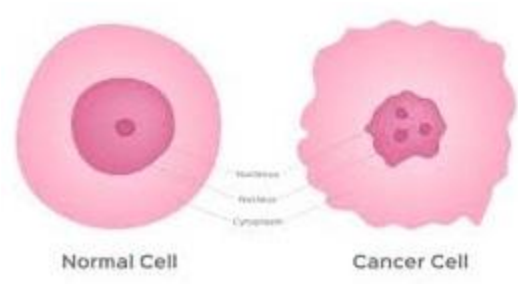


Figure 1. Normal Cells and Cancer cells.

2. Methods

Fractal dimension can track small image shifts that may theoretically provide clinically valuable knowledge about the forms, phases of cancer cells. Mathematical model have been broadly used to show the Cancer cells development. Mathematical model used to clarify the cancer cell growth process. The models are intended to anticipate the pace of progress in the volume of the cancer cells with respect to the change in time t.

2.1. Notations

D	Fractal dimension
δ	Scale size
N_δ	Number of box
$v(t)$	Volume of cells at time t
b	Maximum size
e	exponential
c	Maximum size/minimum size
a	Rate of growth
t	time

2.2. Box counting Dimension

The Box counting method applied to two dimensional point patterns to estimate the cluster dimension with range $1 \leq D \leq 2$. The length of the side δ on the grid of the box counting method. The Number of square box containing lines is N [3]. The length of the side rectangle δ is half, and then the process is repeated. N_δ is the total number of boxes containing rows of a given box size in figure 2. The Fractal dimension D is determined according to the slope of the straight line between the logarithmic graph N_δ and δ, such that [3],

$$N_\delta \propto \delta^{-D} \tag{1}$$

$$D = \frac{\log k - \log (N_\delta)}{\log \delta}. \tag{2}$$

Which is characteristic of the figure maintained by scale. Hence in the limit

$$D = \lim_{r \to 0} - \left\{ \frac{\log (N_\delta)}{\log \delta} \right\} \tag{3}$$

$$D = \lim_{r \to 0} \left\{ \frac{\log (N_\delta)}{\log \delta} \right\} \tag{4}$$

D indicates the degree of complexity or dimension of fractal

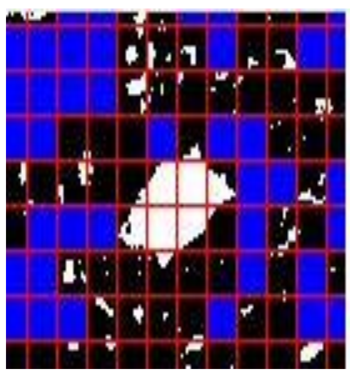


Figure 2. Grid method images.

2.3. HarFA Fractal analysis

Box counting method this method approach is also to decide the dimension of the fractal box in digital fractal structure images. This method measures of fractal properties of normal images was used. The Box counting method in software called HarFa, developed at the Physical and Applied Chemistry Institutes Technical University of Bingo in the Czech republic, has been introduced by Nezadel et al. and Buchnicek et al. The approach for box counting method uses the fractal pattern covered with the box raster and evaluates how many boxes $_{BW}, n_{BBW} = n_B + n_{BW}$ or $n_{WBW} = n_W = n_W + n_{BW}$ of the raster are needed to cover fractal completely [7]. The n is denoted for number of box, B and W is denoted for black and white.

If this calculation is repeated by different size of boxes $r = \frac{1}{\varepsilon}$ the box size r and the number of $n(r)$ boxes required for an absolutely fractal covers will becomes logarithmical. The slope of the liner equation are given by

$$\ln n_{BW}(r) = \ln(k_{BW}) + D_{BW} \ln(r) \tag{5}$$

$$\ln n_{BBW}(r) = \ln(k_{BBW}) + D_{BBW} \ln(r) \tag{6}$$

$$\ln n_{WBW}(r) = \ln(k_{WBW}) + D_{WBW} \ln(r). \tag{7}$$

BW characterizes fractal pattern boundary properties, D_{BBW} characterizes the white background fractal pattern and D_{WBW} characterizes the Black background fractal pattern. We will determine the fractal dimensions of the Cells in Discrete and continuous process from the above program.

2.4. Gompertz Growth Model

This model was introduced by Benjamin Gompertz as an organism growth model. This model shows that the volume of cancer cell decreases with cell death and increases in relation to the surface area. According to this model it predicts the growth of cancer cells. The equation of this model is [8]. The Gompertz equation can be written in the form:

$$\frac{dv}{dt} = a(\ln b - \ln v)v. \tag{8}$$

It can write the equation in differential equation in differential form and integrate as

$$\int \frac{dv}{v\left[\ln\left(\frac{b}{v}\right)\right]} = \int a \cdot dt \tag{9}$$

$$-\ln\left|\ \ln\left(\frac{b}{v}\right)\right| = at + c, \tag{10}$$

where $C = \pm e^{-c}$ is an arbitrary constant

$$\ln\left(\frac{b}{v}\right) = C \cdot e^{-at} \tag{11}$$

$$\frac{b}{v} = e^{c \cdot e^{-at}}. \tag{12}$$

Thus the solution of the Gompertz Growth model

$$v = be^{-c \cdot e^{-at}}. \tag{13}$$

Assume that a Gompertz growth model with constant value $b = 2.6 \times 10^{-6}$, $a = 0.5$ and substituting these value into the equation (10) that it is just obtained gives

$$v(t) = 2.6 \times 10^{-6} e^{-2.6e^{-0.5t}}.$$

2.5. Maximum modulus Theorem

Let $f(z)$ be continuous in closed and bounded region R and analytic and non-constant in the interior of R. Then $|f(z)|$ attains its maximum value on the boundary of R and never in the interior of R.

In analytic tissue, cell growth is constant in a closed bounded region, but it is not constant in the interior tissue. Then the limit can be reached on the tissue's exterior rather than its interior. As a result of the above theorem, we can determine the cancer cell's maximum boundary. The box counting method can be used to prove this method [10].

2.6. Statistical Analysis

A statistical representation of the dispersion of data points across the mean is the coefficient of variation (relative standard deviation). The metric is often used to measure data dispersion between different data sets. Unlike the standard deviation, which must always be viewed in relation to the data's mean, the coefficient of variance is an easy and fast way to compare various data sets [13].

$$\text{Coefficient of variation } = \frac{\sigma}{\mu} \times 100\% \tag{14}$$

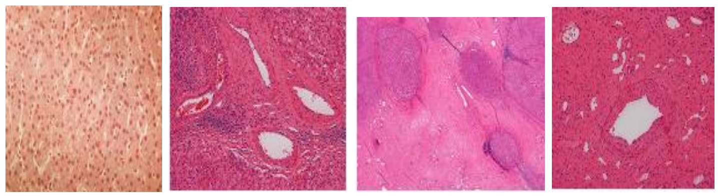
where

$\sigma -$ the Standard deviation

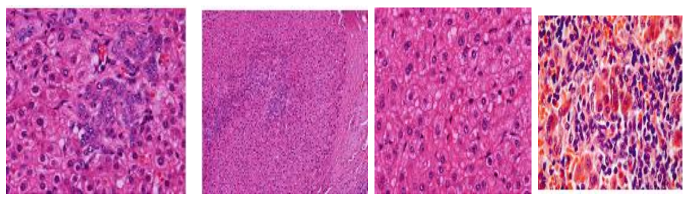
$\mu -$ the mean.

3. Result

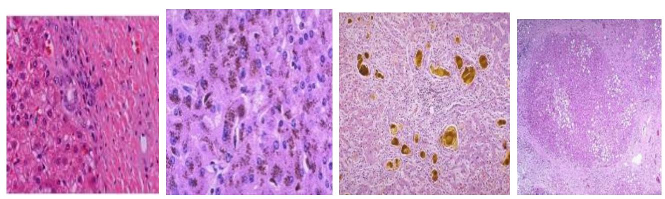
From the figures 3 and 4 represent the microscopic images of Liver Cancer cells and normal cells. To distinguish the cancer cells, Fractal dimension analysis was used specifically the box counting method its approach in figures 4 and 5. It was discovered that normal and cancer cells had significantly different architecture complexity. Cells growth naturally dimension also increases. This dimension of the cells can be found by Box counting method. Table 1 and Table 2 show the dimension of the normal and Cancer cells. The above method is applied for various images. This was programming in Image *j* software. If the cells dimension are 0.33, 0.381 then cells are like ordinary tissue and the initial phases. If the cell dimension is like 1.370, 1.441 cells like moderate tissue is a second phase. The cells are like advanced tissue because the dimension of cells such as 1.909, 1.953 are cancer cells. This method is helpful to identifying cancer grade levels. Using HarFA Fractal analysis software and the box counting method, we determine the intensity of the cells. The box-counting method uses the raster-boxed covering patterns to assess how many n_{BW}, n_{BBW} and n_{WBW} of the raster are needed to cover fractal complexity. For different pictures, we did this process. The values of B_W, B, $B + B_W$ are denoted Perimeter, area, total area of the normal and cancer cells for discrete and continuous processes are shown in Tables 3 and 4. The density of the cells in the liver organ is seen here. Higher dimensions indicate a higher grade, while lower dimensions indicate a lower grade. Mathematical model of cell growth, Table 5 represents the cells growth to predict normal and abnormal cells. The cells growth rate is differ from human to human. Its value can reach more than 2.6 micrometer in its advanced stage. By the Maximum modulus theorem, the cell growth is continuously reach its maximum boundary. Maximum value to give the maximum dimension. The Statistical analysis applying in the normal cells and Cancer cells to get the growth pattern of higher consistent.



I_1 I_2 I_3 I_4

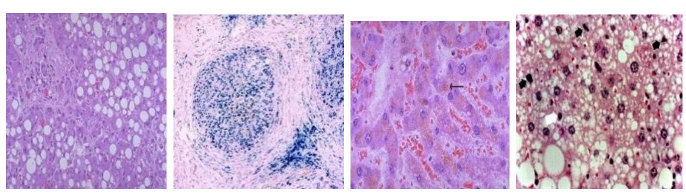


I_5 I_6 I_7 I_8

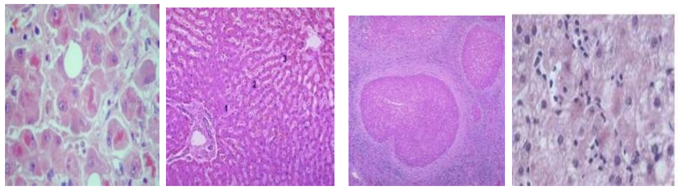


I_9 I_{10} I_{11} I_{12}

Figure 3. Cancer cell images of Liver (Hepatocytes).



I_{13} I_{14} I_{15} I_{16}



I_{17} I_{18} I_{19} I_{20}

Figure 4. Normal cell images Liver (Hepatocytes).

Table 1. Cancer cells at different scaling in Fractal Dimension.

Image	Scaling									D_B
	2	3	4	5	6	7	8	9	10	
I_1	1.896	1.759	1.935	1.799	1.812	1.861	1.845	1.868	1.725	1.833
I_2	1.245	1.356	1.352	1.725	0.985	1.480	1.414	1.425	1.352	1.370
I_3	1.414	1.352	1.244	1.491	1.344	1.581	1.403	1.543	1.625	1.441
I_4	1.285	1.342	1.244	1.571	1.576	1.656	1.690	1.544	1.674	1.509
I_5	1.822	1.942	1.963	1.952	1.841	1.987	1.985	1.925	1.933	1.953
I_6	1.974	1.141	1.532	1.285	1.421	1.342	1.316	1.426	1.254	1.410
I_7	1.869	1.975	1.535	1.793	1.832	1.681	1.784	1.745	1.532	1.749
I_8	1.845	1.956	1.752	1.825	1.975	1.848	1.841	1.826	1.847	1.857
I_9	1.814	1.652	1.774	1.871	1.714	1.751	1.706	1.777	1.736	1.755
I_{10}	1.852	1.634	1.734	1.671	1.676	1.926	1.793	1.711	1.752	1.749
I_{11}	1.822	1.941	1.963	1.954	1.844	1.922	1.965	1.853	1.921	1.909
I_{12}	1.574	1.641	1.532	1.685	1.711	1.642	1.616	1.562	1.753	1.635

Table 2. Normal cells at different scaling in Fractal Dimension.

Image	Scaling									D_B
	2	3	4	5	6	7	8	9	10	
I_{13}	0.912	0.866	0.750	0.672	0.466	0.342	0.262	0.265	0.210	0.527
I_{14}	0.921	0.913	0.766	0.688	0.478	0.315	0.296	0.296	0.254	0.547
I_{15}	0.953	0.806	0.706	0.650	0.451	0.331	0.254	0.275	0.216	0.515
I_{16}	0.632	0.592	0.489	0.359	0.275	0.217	0.176	0.145	0.154	0.330
I_{17}	0.822	0.942	0.963	0.952	0.841	0.987	0.985	0.845	0.866	0.911
I_{18}	0.339	0.655	0.871	0.630	0.444	0.339	0.218	0.349	0.33	0.463
I_{19}	0.403	0.821	0.771	0.655	0.456	0.336	0.254	0.213	0.280	0.465
I_{20}	0.377	0.764	0.652	0.459	0.336	0.239	0.210	0.200	0.197	0.381

Table 3. HarFA Fractal Analysis of Cancer cells in Liver (Hepatocytes).

Image	Discrete			Continuous		
	B_W	B	$B+B_W$	B_W	B	$B+B_W$
I_1	1.44	0.018	1.458	1.688	0.181	1.869
I_2	1.456	0.121	1.577	1.825	0.020	1.845
I_3	1.459	0.104	1.563	1.651	0.163	1.814
I_4	1.652	0.140	1.792	1.701	0.151	1.852
I_5	1.351	0.272	1.623	1.858	0.064	1.922
I_6	1.331	0.335	1.666	1.854	0.120	1.974
I_7	1.359	0.165	1.524	1.802	0.023	1.825
I_8	1.345	0.021	1.366	1.892	0.079	1.971
I_9	1.476	0.150	1.622	1.856	0.115	1.971
I_{10}	1.489	0.095	1.584	1.922	0.032	1.954
I_{11}	1.451	1.623	1.968	1.934	1.685	1.642
I_{12}	1.478	1.599	1.764	1.952	1.922	1.946

Table 4. HarFA Fractal Analysis of Normal cells in Liver (Hepatocytes).

Image	Discrete				Continuous		
	B_W	B	$B+B_W$		B_W	B	$B+B_W$
I_{13}	0.662	0.118	0.780		0.589	0.085	0.674
I_{14}	0.546	0.228	0.774		0.325	0.445	0.770
I_{15}	0.740	0.124	0.864		0.651	0.132	0.783
I_{16}	0.673	0.095	0.768		0.700	0.074	0.774
I_{17}	0.354	0.107	0.461		0.685	0.084	0.769
I_{18}	0.547	0.349	0.654		0.547	0.349	0.896
I_{19}	0.865	0.098	0.960		0.630	0.171	0.801
I_{20}	0.870	0.105	0.975		0.699	0.091	0.790

Table 5. Mathematical model of cancer cell growth in Different timeand Growth rate.

Time(years)	$a = 0.5$	$a = 0.6$	$a = 0.7$
5 month	0.494	0.351	0.373
1 years	1.023	0.624	0.715
1 year 8 month	1.274	1.003	1.153
2 years 6month	1.85	1.455	1.657
3 years	2.16	1.69	1.893
5 years	2.386	2.88	2.40

4. Conclusion

In this paper we have proposed a Mathematical model to analysis the growth of normal and cancer cells. Dimension of fractal is an essential method for discovering tissue cells. Fractal analyses on the shape and size of the digital cell images. Our measurement specifically demonstrates that the normal and abnormal cells vary significantly. The structure and scale of cells vary amongst humans. This cell-form complexity measurement dimension. To may confirm the cancer stage from these images, Pathologist can be helpful in diagnosing cancer cells development.

References

[1] Mandelbrot, The Fractal Geometry of nature, W. H. Freeman (San Francisco, 1983).

[2] N. C. Kenkel and D. J. Walker, Fractal in the Biological Sciences, Coenoses 11: 77-100 (1996).

[3] James W. Baish and Rakesh K. Jain, Fractal and cancer, Cancer Research 60 July 15 (2000), 3683-3688.

[4] Weiwei Pei and Jiayo Chen, Regional bio medical imaging of liver cancer cells, Journal of Cancer 10(19) (2019), 4481-4487.

[5] Vinay G. Vaidya and Frank J. Alexandro JR, Evaluation of some mathematical models for tumor growth, International Journal of Biomedical Computing (13) (1982), 19-35.

[6] James Stewart and Troy Day, Bio-calculus: for the life science, Cengage Learning Publication, 2015.

[7] R. Uthaya Kumar and G. Jayalalitha, Border Detection of skin cancer cells with fractal dimension, World Scientific Publishing Company, Fractals 17(2) (2002), 171-180.

[8] Alan, Gar Finkel, Jane Shevtsov and Yino Guo, Modelling life: The Mathematics of biological systems, Springer International Publishing, 2017.

[9] Eva Ostertagova and Oskar Ostertag, Methodology and Application of One-way ANOVA, American Journal of Mechanical Engineering 1(7) (2013), 256-261.

[10] James Ward Brown and Ruel V. Churchill, Complex variable and applications, Eighth edition, McGraw-Hill Higher Education Publication, 2009.

[11] Anne Talkington and Rick Durrett, Estimating Tumor Growth Rates in Vivo, Bulletin Mathematical Biology, 2015.

[12] R. B. Ogunrinde and S. O. Ayinde, Interpolating and Gompertz function approach in tumour growth analysis, American Journal of Mathematics and Statistics 8(5) (2018), 119-125.

[13] S. C. Gupta and V. K. Kapoor, Fundamentals of Mathematical Statistics, Sultan Chand and Sons Educational Publishers, Edition, 2002.