Cancer Cell Growth Under Radiotherapy Using Stochastic Model

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Abstract: A malignant (Cancer) cell is once formed in the human body then it will grow as a tumor by a proliferation of cells. To control the cancer cell growth radiotherapy is one of the medically adopted methods, which is prescribed on a cyclic basis. When a radiation is introduce to the body, both normal and mutant cells are killed. Life-threatening hazards may develop due to either long-time administration or short time radiation administration leads to the loss of white blood cells or growth of tumor size respectively. It is acknowledge that the process of cell growth and destruction square measure random. Keeping this in mind a stochastic model was developed to study the cancer cell growth under radiotherapy as well as the under-recovery state. The Laplace transformation of the tumor size distribution under transient conditions is derived. The equilibrium probabilities of tumor size both in radiotherapy and recovery states were derived. The probability of extinction of the tumor, the average, and variance of the number of cancer cells in the tumor was derived. These models are useful for obtaining the radiation therapy spells with minimum risk.

Index Terms: Radiotherapy, Growth of tumor, Laplace Transformation, Stochastic process, Birth and death process, Stochastic modeling.

1 INTRODUCTION

Radiotherapy may be a medical treatment for the management of neoplastic cell growth through medication. Malignant tumors (cancer) tends to grow apace and show variations in size and form. The radiation therapy is prescribed on a cyclic basis. Once an associate anti-tumor drug is evoked to the body, each traditional and cancer cells square measure killed. The white blood cells fall to the lower level and care is required to gauge the standing of the patient. If the outcome back is not favorable, life-threatening hazards could develop therefore; the associated interval of your time is to be such that throughout that the therapy could also be out of print to recover. However, because of the ending of therapy, the growth will grow. At the top of this recovery amounts, the therapy is to be started once more. Iverson et.al (1950) delineate the expansion of remodeled cell, an antecedent of growth by a pure linear birth method. D.G.Kendall (1960), Neyman et al (1967) have developed a random model for Carcinogenesis mistreatment birth and death method to explain growth. Wette et al (1974) have developed a density-dependent birth and death framework for the growth of solid tumors primarily based upon the Physical characteristics and medicine responses. B.G.Birkhead (1986) developed random models for neoplastic cell growth viewing that the method of growth and mutation of cells square measure, Poisson. Dewanjii et al. (1989, 1991) have developed a random model for cancer risk assessment through the quantity and size of the malignant clones. Lover (1990) reviewed varied mathematical model for cancer therapy issues and to see optimum drug regimes. However, a very little work has been according to relating to the neoplastic cell growth throughout the periods of presence and absence of therapy because of the random nature of the constituent method, things were to be analyzed through random modeling of cancer cells throughout the therapy and its absence. It is assumed that the loss method of the malignant cells follows the Poisson method with completely different parameters, once the patient is below therapy and once the patient is in a recovery state. Equally, the expansion method of the cancer cells is additionally Poisson with completely different parameters for two states of the patient. It is conjointly assumed that the recovery periods square measure severally and identically distributed exponential variate s. With these concerns, during this chapter, we tend to develop a random model for neoplastic cell growth that is far helpful for determinant the optimum drug dose regimes.

2 STOCHASTIC MODEL

Let the growth of the cancer cells is Poisson with growth rates ‘o’ and ‘nλ’ during the presence of radiotherapy and in the absence of radiotherapy respectively. The time for which the patient is in recovery state is exponentially distributed with parameters (excess lifetime). The time in which the patient is under the radiotherapy treatment is a random variable with probability density function f(x). If δcr(x) is the conditional probability that the patient will move from the radiotherapy state to recovery state given that the patient has been under treatment for a time ‘x’ i.e hazard rate function is

δcr(x) = \frac{f(x)}{1 - \int_0^x f(y)dy}

So, the probability density function is given by

f(x) = δcr(x) e^{-\int_0^x δcr(y)dy}

Also, assume that the loss process of cancer cells is Poisson with death rates ‘nμ’ and ‘nμ’ when the patient is under recovery and under the radiotherapy states respectively. Let the maximum size of tumor (number of cells in the tumor) be N.

Let Pr,n(t) be the probability that the patient is under recovery state and there are ‘n’ cancer cells present in the tumor at time ‘t’ and Pr,n(t,x) be the probability that the patient is under the treatment of radiotherapy and ‘n’ cancer cells are present in the tumor at time ‘t’ and has been in the recovery state for the period of time, (x, x + dx).

With the above assumptions, The Kolmogorov forward equations of the model are Karlin and Taylor 1975,

\begin{align*}
P_{r,0}(t + h) &= (1 - \lambda h - \delta_{r,1}h)P_{r,0}(t) + \mu^*hP_{r,1}(t) \\
&+ \int_0^\infty \delta_{cr}(x) hP_{c,0}(t,x) dx(1)
\end{align*}
With the boundary conditions, 
\[ p_{cn}(0) = 1 \text{ for } n = 0 \]
\[ p_{cn}(o, x) = 0 \text{ for all } n \geq 0; p_{cn}(t, 0) = \delta_{cr}P_{r,n}(t), \text{ forn} \leq N \]

The Kolmogorov forward equations of the model are
\[
\frac{d}{dt}P_{r,n}(t) = -(\lambda + \delta_{rc})P_{r,n}(t) + \mu_{r}P_{r,1}(t)
\]
\[ + \int_{0}^{\infty} \delta_{cr}(x)P_{c,0}(t, x)dx \]
\[
\frac{d}{dt}P_{r,n}(t) = -n\lambda + \mu_{r}P_{r,1}(t) + (n + 1)\mu_{r}P_{r,(n+1)}(t)
\]
\[ + (n + 1)\lambda P_{r,n-1}(t)
\]
\[ + \int_{0}^{\infty} \delta_{cr}(x)P_{c,n}(t, x)dx \]
\[ \text{for } 1 \leq n \leq N - 1 \] (7)

\[
\frac{d}{dt}P_{r,n}(t) = -(n\lambda + \delta_{rc})P_{r,n}(t) + (n + 1)\mu_{r}P_{r,(n+1)}(t)
\]
\[ + (n + 1)\lambda P_{r,n-1}(t)
\]
\[ + \int_{0}^{\infty} \delta_{cr}(x)P_{c,n}(t, x)dx \]
\[ \text{for } 1 \leq n \leq N - 1 \] (8)

For solving these equations, we use Laplace transformation. Multiplying the equation (7) with \( e^{-st} \) on both sides and integrating, we have
\[
\frac{d}{dt} \int_{0}^{\infty} e^{-st}P_{r,0}(t)dt = -(\lambda + \delta_{rc}) \int_{0}^{\infty} e^{-st}P_{r,0}(t)dt
\]
\[ + \mu_{r} \int_{0}^{\infty} e^{-st}P_{r,1}(t)dt
\]
\[ + \int_{0}^{\infty} (\delta_{cr}(x))P_{c,0}(t, x)e^{-st}dx \]
\[ \text{for } s + \lambda + \delta_{rc} \neq 0 \] (13)

Denoting \( \bar{P}_{r,0}(s) = \int_{0}^{\infty} e^{-st}P_{r,0}(t)dt \), which is Laplace transformation of \( P_{r,0}(t) \) and substituting in the equation (13) and after some simplification, we have
\[
\bar{S}_{P_{r,0}}(s) = -(\lambda + \delta_{rc})\bar{P}_{r,0}(s) + \mu_{r}P_{r,1}(s)
\]
\[ + \int_{0}^{\infty} (\delta_{cr}(x))\bar{P}_{c,0}(s, x)dx \]

Using the boundary condition and on simplification, we get
\[
(\lambda + \delta_{rc})\bar{P}_{r,0}(s) = 1 + \mu_{r}P_{r,1}(s)
\]
\[ + \int_{0}^{\infty} (\delta_{rc}(x))\bar{P}_{c,0}(s, x)dx \]
\[ \text{for } s + \lambda + \delta_{rc} \neq 0 \] (15)

Considering the equation (8) to (12) and taking the Laplace transformation and using the boundary conditions, we have
\[
(s + \lambda + \delta_{rc} + n\mu_{r})\bar{P}_{r,n}(s) = (n + 1)\mu_{r}P_{r,n+1}(s) + (n + 1)\lambda P_{r,n-1}(s)
\]
\[ + \int_{0}^{\infty} (\delta_{cr}(x))\bar{P}_{c,n}(s, x)dx, \quad 1 \leq n \leq N - 1 \]
\[
(s + \delta_{rc}(x))\bar{P}_{c,0}(s, x) = \mu_{r}P_{c,1}(s, x) - \frac{\partial}{\partial x} \bar{P}_{c,0}(s, x)
\]
\[ (s + n\mu_{r} + \delta_{cr}(x))\bar{P}_{c,n}(s, x) = (n + 1)\mu_{r}P_{c,n+1}(s, x) - \frac{\partial}{\partial x} \bar{P}_{c,n}(s, x), \quad 1 \leq n \leq N - 1 \]
\[ (s + \lambda + \delta_{rc}(x))\bar{P}_{c,N-1}(s, x) = \frac{\partial}{\partial x} \bar{P}_{c,N-1}(s, x) \]
\[ \text{for } s + \lambda + \delta_{rc} \neq 0 \] (16)

Solving the linear differential equation (20), we get
\[
\bar{P}_{c,n}(s, x) = \bar{P}_{c,0}(s, x)e^{-(s + n\mu_{r})x - \int_{0}^{x} \delta_{cr}(x)dx}
\]
\[ \bar{P}(s, x) = \bar{P}_{c,0}(s, 0)[1 - F(x)]e^{-(s + n\mu_{r})x} \]
\[ F(x) = \int_{0}^{x} f(y)dy \]
\[ \text{for } s + \lambda + \delta_{rc} \neq 0 \] (21)

Taking \( n = N - 1 \) in the equation (19), we have
\[
\frac{\partial}{\partial x} \bar{P}_{c,N-1}(s, x) + (s + (N - 1)\mu_{r} + \delta_{cr}(x))\bar{P}_{c,N-1}(s, x) = 0
\]
\[ \text{for } s + (N - 1)\mu_{r} + \delta_{cr}(x) \neq 0 \] (22)

Using (21) and solving the equation (20), we get
\[
\bar{P}_{c,N-1}(s, x) = N\mu_{r}\bar{A}_{1}\bar{P}_{c,N}(s, 0) + \bar{P}_{c,N-1}(s, 0)e^{-(s + (N - 1)\mu_{r})x - \int_{0}^{x} \delta_{cr}(x)dx}
\]
Where, \( \bar{A}_{1} = \frac{e^{-(\mu_{r})x}}{2(\mu_{r})^{2}} \)

Taking \( n = N - 2 \) in the equation (19), we have
\[
\bar{P}_{c,N-2}(x, s) = [N(N - 1)\mu_{r}\bar{A}_{2}\bar{P}_{c,N}(s, 0) + (N - 1)\mu_{r}^{2}\bar{P}_{c,N-1}(s, 0)\bar{A}_{1} + \bar{P}_{c,N-2}(s, 0)]e^{-(s + (N - 2)\mu_{r})x - \int_{0}^{x} \delta_{cr}(x)dx}
\]
Where, \( \bar{A}_{1} = \frac{e^{-(\mu_{r})x}}{2(\mu_{r})^{2}} \) and for \( 1 \leq i \leq N - 1 \)
\[
\bar{P}_{c,N-i}(x, s) = \sum_{k=0}^{i} \binom{N-i}{k} \mu_{r}^{-k+1-i} \bar{A}_{i-k}\bar{P}_{c,N-k}(s, 0)e^{-(s + (N - i)\mu_{r})x - \int_{0}^{x} \delta_{cr}(x)dx}
\]
Where, \( \bar{A}_{0} = 1 \) and \( \bar{A}_{i} = (-i)\left(\frac{(\mu_{r})^{i}x}{k!(\mu_{r})^{k}}\right) \)
\[
\binom{N-k}{i} = \frac{(N-K)!}{(N-i)!}
\]
\[ (N-k)!(N-i)! \] (25)
Taking $i = N - 1$ we have

$$
\bar{P}_{c,1}(s, x) = \sum_{k=0}^{N-1} \binom{N-k}{p} \left( N - k \right) \bar{P}_{c,N-k}(s, x)
$$

(26)

Substituting the value of $\bar{P}_{c,1}(s, x)$ from the equation 26 in the equation 18

We have

$$
\bar{P}_{c,0}(s, x) = \sum_{k=0}^{N-1} \binom{N-k}{p} \left( N - k \right) \bar{P}_{c,N-k}(s, x)
$$

(27)

By taking $(N - i) = n$ in equation (25) we have

$$
\bar{P}_{c,n}(s, x) = \sum_{k=0}^{n} \binom{N-k}{p} \left( N - k \right) \left( \mu^v \right)^{N-k} \bar{A}_{N-k-1} \bar{P}_{c,N-k}(s, x)
$$

(28)

Where, $\bar{A}_{k}$ is as given in the equation (25)

Substituting the value of $\bar{P}_{c,n}(s, x)$ from the equation (27) in the equation (18) and using the boundary conditions, we get $\bar{P}_{c,0}(s)$

Therefore

$$
\bar{P}_{c,0}(s) = \int_{0}^{\infty} \delta(x) e^{-\int_{0}^{x} \delta_{cr}(x) dx} dx
$$

(29)

$L$ is the Laplace transform operator.

Substituting the value of $\bar{P}_{c,n}(s, x)$ from the equation (28) in the equation (16) and using the boundary conditions, we get

$\bar{P}_{c,0}(s)$

(30)

On simplification we have

$\bar{P}_{c,0}(s) = \int_{0}^{\infty} \delta(x) e^{-\int_{0}^{x} \delta_{cr}(x) dx} dx$

(31)

This implies

$\bar{P}_{c,0}(s) = \int_{0}^{\infty} \delta(x) e^{-\int_{0}^{x} \delta_{cr}(x) dx} dx$

(32)

Where

$$
\left( \frac{N - r - k}{C} \right) = \left( \frac{N - r - k}{C} \right) \left( \frac{N - r - k}{C} \right)
$$

Substituting the value of $\bar{P}_{c,n}(s)$ in equation (17) and using the boundary conditions we have

$\bar{P}_{c,n}(s) = (N - 1) \lambda \bar{P}_{r,n-1}(s)$

(33)

This implies

$$
\left( s + \mu \right) \bar{P}_{r,n-1}(s) + \bar{P}_{r,0}(s)
$$

(34)

The equation (34) can be written as

$$
\bar{P}_{r,0}(s) = (A_1 - 1) \bar{P}_{r,0}(s)
$$

Where,

$A_1 = \frac{1}{1 - \lambda} \left( s + \mu \right)$

(35)

Taking $n = N - 1, N - 2, ..., n$ in equation (32)

$\bar{P}_{r,N-2}(s) = A_2 \bar{P}_{r,N-1}(s)$

This implies

$$
\bar{P}_{r,N-2}(s) = K_3 \bar{P}_{r,N-2}(s)
$$

(36)

Where

$K_3 = A_3 \left( A_1 - 1 \right) - B_3 \bar{P}_{r,N-1}(s)$

In general $\bar{P}_{r,N-k}(s) = K_3 \bar{P}_{r,N-k}(s)$ for $2 \leq k \leq N$

Where

$K_3 = \left( A_1 - 1 \right) - B_3 \lambda

(37)

The equation (37) gives the values of $\bar{P}_{r,N-k}(s)$ in terms of $\bar{P}_{r,0}(s)$.

We can obtain $\bar{P}_{r,n}(s)$ as

$$
\bar{P}_{r,n}(s) = \int_{0}^{\infty} \delta(x) e^{-\int_{0}^{x} \delta_{cr}(x) dx} dx
$$

(38)

Where

$$
\sum_{k=0}^{N-n} \binom{N-k}{C} \left( s + \mu \right) \bar{P}_{r,N-k}(s)
$$

and $K_n$ as given in the equation (37).

The Laplace transform of the probability that at time $t$ there are $(N - i)$ malignant cells in the tumor when the patient is under radiotherapy is obtained
On simplification, we get

\[
P_{c,N-i}(s) = \sum_{k=0}^{i} \binom{N-k}{i-k} \frac{1}{i!} \sum_{l=0}^{i-k} \frac{(-1)^{i-k}}{l} \left[ \frac{1 - \bar{f}(s_{N-i-l})}{s_{N-i-l}} \right]
\]

Using the boundary conditions, we have

\[
P_{c,0}(s) = \sum_{k=0}^{N} \left( \sum_{i=0}^{N-k} \binom{N-k}{i-k} K_k \sum_{l=0}^{N-k} \frac{(-1)^{i-k}}{l} \left[ \frac{1 - \bar{f}(s_{N-k-l})}{s_{N-k-l}} \right] + \sum_{i=0}^{N} \left( \frac{N-k}{i!} \delta_{rc} \sum_{l=0}^{i} \frac{(-1)^{i-k}}{l} \left[ \frac{1 - \bar{f}(s_{N-i-l})}{s_{N-i-l}} \right] \right) \right)
\]

Using the boundary conditions, we have

\[
P_{c,N-i}(s) = \sum_{k=0}^{i} \binom{N-k}{i} \frac{1}{i!} \sum_{l=0}^{i-k} \frac{(-1)^{i-k}}{l} \left[ \frac{1 - \bar{f}(s_{N-i-l})}{s_{N-i-l}} \right] + \sum_{k=0}^{N} \left( \sum_{i=0}^{N-k} \binom{N-k}{i-k} \frac{1}{i!} \sum_{l=0}^{i} \frac{(-1)^{i-k}}{l} \left[ \frac{1 - \bar{f}(s_{N-i-l})}{s_{N-i-l}} \right] \right)
\]

3 LIMITING BEHAVIOR OF THE MODEL

Assuming that the tumor is in the equilibrium state and applying Tauberian theorem, we have

\[
\lim_{s \to 0} sF(s) = \lim_{t \to 0} F(t), \lim_{t \to 0} P_{r,n}(t) = P_{r,n} \text{and} \lim_{t \to 0} P_{c,n}(t) = P_{c,n}
\]

The equilibrium probabilities of the tumor size when the patient is under radiotherapy is obtained as
\[
\begin{align*}
[P_{r,N}]^{-1} &= 1 + \sum_{k=1}^{N} K_k \\
&+ \sum_{i=1}^{N-1} \left( \frac{p}{l} \right) \delta_{rc} \sum_{i=0}^{i-1} \left( \begin{array}{c} N \ \\
N-i \end{array} \right) (-1)^{i+1} \left( 1 - \frac{1}{(N-i)\mu^c} \right) \\
&+ (1) \left( \frac{N-1}{p} \right) \sum_{i=0}^{i-1} \left( \begin{array}{c} i-1 \ \\
l \end{array} \right) (-1)^{i+1} \left( 1 - \frac{1}{(N-i)\mu^c} \right) \\
&- \varphi_{l,0} \left( \frac{N-k}{p} \right) \sum_{i=0}^{i-1} \left( \begin{array}{c} i-k \ \\
i \end{array} \right) (-1)^{i+1} \left( 1 - \frac{1}{(N-k)\mu^c} \right) \\
&+ \sum_{k=2}^{i} \left( \frac{N-k}{p} \right) \delta_{rc} K_k \sum_{i=0}^{i-k} \left( \begin{array}{c} i-k \ \\
i \end{array} \right) (-1)^{i+1} \left( 1 - \frac{1}{(N-k-i)\mu^c} \right) \\
&+ \delta_{rc} K_N m_f
\end{align*}
\]

Where,
\[
A_k = \frac{1}{(N-k)\lambda} \left( \frac{N-k+1}{\mu^r} + \frac{N-k+1}{\mu^c} + \delta_{rc} \bar{f}_{(N-k+1)\mu^c} \right)
\]
\[
B_k = \frac{1}{(N-k)\lambda} \left( \frac{N-k+2}{\mu^r} + \delta_{rc} \left( \frac{N-k+2}{\mu^c} \right) \bar{f}_{(N-k+2)\mu^c} \right)
\]
\[
D_k = \frac{1}{(N-k)\lambda} \left( \sum_{i=0}^{i-k} (-1)^{i+1} (N-1) \left( \begin{array}{c} N-1 \ \\
k-l-1 \end{array} \right) \delta_{rc} \right)
\]

4 MODEL BEHAVIOUR WHEN THE CYCLE LENGTH IS EXPONENTIAL

Since the distribution of the tumor size depends on the random time \(X\), during which the patient is under radiotherapy, let us assume that it follows an exponential distribution with parameter \(\delta_{rc}\). Then the transition probability from presence of radiotherapy to the recovery state \(\delta_{rc}(x)\) becomes \(\delta_{rc}\)

\[
\bar{f}(s_i) = \int_{0}^{\infty} \delta_{rc} e^{-(s_1+\delta_{rc})x} dx = \frac{\delta_{rc}}{\delta_{rc} + s_1}
\]

We have
\[
P_{c,N-1}(s) = (A_1 - 1)\bar{P}_{r,N}(s)
\]
\[
P_{c,N-k}(s) = K_k\bar{P}_{r,N}(s), \quad 2 \leq k \leq N;
\]
\[
[P_{r,N}]^{-1} = \{s + \lambda + \delta_{rc} \bar{f}(s)\} - K_N - \mu^r K_{N-1}
\]

\[
- \delta_{rc} \sum_{k=0}^{N-1} \left( \begin{array}{c} N-k \ \\
N-k-1 \end{array} \right) (\mu^c)^{N-k} K_k L(\bar{A}_{N-k}(\alpha)) f(x)
\]

Where \(K_k\) and \(\bar{A}_{N-k}\) are as given in the equations (37) and (38).

When the patients is under radiotherapy, we have

\[
\frac{1 - \bar{f}(s_i)}{s_1} = \frac{1}{\delta_{rc} + s_1}
\]

This implies
\[
[P_{c,N-1}(s)]^{-1} = \sum_{i=1}^{N-1} \left( \begin{array}{c} N \ \\
i \end{array} \right) \delta_{rc} \sum_{i=0}^{i-1} \left( \begin{array}{c} i \ \\
l \end{array} \right) (-1)^{i+1} \left( \frac{1}{\delta_{rc} + s_{N-1}} \right)
\]

\[
+ (1 - \varphi_{l,0}) \left( \frac{N-k}{p} \right) \sum_{i=0}^{i-1} \left( \begin{array}{c} i-k \ \\
i \end{array} \right) (-1)^{i+1} \left( \frac{1}{\delta_{rc} + s_{N-k}} \right)
\]

\[
+ \sum_{k=2}^{i} \left( \frac{N-k}{p} \right) \delta_{rc} K_k \sum_{i=0}^{i-k} \left( \begin{array}{c} i-k \ \\
i \end{array} \right) (-1)^{i+1} \left( \frac{1}{\delta_{rc} + s_{N-k}} \right)
\]

\[
\bar{P}_{r,N}(s)
\]

Where \(s_n = s + n(\mu^c)\)

\[
\bar{P}_{c,0}(s) = \sum_{k=0}^{N-1} \left( \frac{N}{N-k} \right) \delta_{rc} K_k \sum_{i=0}^{i-1} \left( \begin{array}{c} i \ \\
l \end{array} \right) (-1)^{i+1} \left( \frac{1}{\delta_{rc} + s_{N-k}} \right)
\]

Where

\[
A_1 = \frac{1}{(N-1)\lambda} \left( s + N\mu^r + (N-1)\lambda + \delta_{rc} - \delta_{rc} \left( \frac{\delta_{rc}}{\delta_{rc} + s_{N-1}} \right) \right)
\]

\[
A_k = \frac{1}{(N-k)\lambda} \left( s + (N-k+1)\mu^r + (N-k+1)\lambda + \delta_{rc} \right)
\]

\[
- \delta_{rc} \left( \frac{\delta_{rc}}{\delta_{rc} + s_{N-k}} \right); \quad 2 \leq k \leq N
\]

\[
B_k = \frac{1}{(N-k)\lambda} \left( (N-k+2)\mu^r \right)
\]

\[
- \delta_{rc} \left( \frac{\delta_{rc}}{\delta_{rc} + s_{N-k}} \right)
\]

\[
D_k = \frac{1}{(N-k)\lambda} \left( \sum_{i=0}^{i-k} (-1)^{i+1} (N-1) \left( \begin{array}{c} N-1 \ \\
k-l-1 \end{array} \right) \delta_{rc} \right)
\]

\[
\left\{ \sum_{i=0}^{i-k} \left( \begin{array}{c} i-k \ \\
l \end{array} \right) \left( \frac{\delta_{rc}}{\delta_{rc} + s_{N-j-k}} \right) \right\}
\]

The probability that the patient is under radiotherapy and \((N-i)\) cancer cells are in the tumor at any arbitrary time after reaching the equilibrium position is denoted as \(P_{c,N-i}\).
\[ P_{c,N-i} = \sum_{i=1}^{N-1} \binom{N}{i} \frac{p}{l!} \delta_{rc} \sum_{i=0}^{i} \binom{i}{c} (-1)^{i+1} \left[ \frac{1}{\delta_{cr} + (N - 1)\mu^c} \right] \\
+ \left( 1 - \varphi_{l,0} \right) \binom{N}{i-1} \frac{p}{l!} \delta_{rc} \sum_{i=0}^{i} \binom{i-1}{c} (-1)^{i+1} \left[ \frac{1}{\delta_{cr} + (N - 1 - l)\mu^c} \right] \\
+ \sum_{k=2}^{i} \binom{N-k}{i-k} \delta_{rc} K_k \sum_{i=0}^{i} \binom{i-k}{c} (-1)^{i+k} \left[ \frac{1}{\delta_{cr} + (N - k - l)\mu^c} \right] \right) P_{r,N} \\
+ \delta_{rc} K_NM_f \left( P_{r,N} \right) \right) \\
(54) \\
\]

Where, \( m_f \) is as given in the equation (44).

When the patient is in recovery state. We can obtain the probability that there are \((N - r)\) cancer cells in the tumor as

\[ P_{r,N-1} = (A_1 - 1)P_{r,N}; \quad P_{r,N-k} = K_kP_{r,N} \]

Where \( K_k \) is as given in the equation (37) and

\[ [P_{r,N}]^{-1} = 1 + \sum_{k=1}^{N} K_k \\
+ \sum_{i=0}^{N-1} \binom{N}{i} \frac{p}{l!} \delta_{rc} \sum_{i=0}^{i} \binom{i}{c} (-1)^{i+1} \left[ \frac{1}{\delta_{cr} + (N - l)\mu^c} \right] \\
+ \left( 1 - \varphi_{l,0} \right) \binom{N}{i-1} \frac{p}{l!} \delta_{rc} \sum_{i=0}^{i} \binom{i-1}{c} (-1)^{i+1} \left[ \frac{1}{\delta_{cr} + (N - l - 1)\mu^c} \right] \\
+ \sum_{k=1}^{i} \binom{N-k}{i-k} \delta_{rc} K_k \sum_{i=0}^{i} \binom{i-k}{c} (-1)^{i+k} \left[ \frac{1}{\delta_{cr} + (N - k - l)\mu^c} \right] \right) \]

\[ \sum_{k=0}^{N} \binom{N-k-1}{(N-k)!} \left( \frac{P}{(N-k)!} \right) \delta_{rc} K_k \sum_{i=0}^{i} \binom{i-k}{c} (-1)^{i+k} \left[ \frac{1}{\delta_{cr} + (N - k - l)\mu^c} \right] \]

\[ \sum_{k=0}^{N} \binom{N-k}{(N-k)!} \delta_{rc} K_k \sum_{i=0}^{i} \binom{i-k}{c} (-1)^{i+k} \left[ \frac{1}{\delta_{cr} + (N - k - l)\mu^c} \right] + \delta_{rc} K_NM_f \]

Where,

\[ A_1 = \frac{1}{(N - 1)\lambda} \left( (N - 1)\mu^r + (N - 1)\lambda + \delta_{rc} \frac{1}{\delta_{cr} + N\mu^r} \right) \]

\[ A_k = \frac{1}{(N-k)\lambda} \left( (N-k+1)\mu^r + (N-k+1)\lambda + \delta_{rc} \frac{1}{\delta_{cr} + (N-k+1)\mu^c} \right) \]

\[ 2 \leq r \leq N \]

\[ B_k = \frac{1}{(N-k)\lambda} \left( (N-k+2)\mu^r - \delta_{rc}(N-k+2)P_{r,1} \left( \frac{\delta_{cr}}{\delta_{cr} + (N-k+2)\mu^c} \right) \right) \]

\[ D_k = \frac{1}{(N-k)\lambda} \sum_{j=0}^{k-3} (-1)^{k-j} \binom{N-j}{k-j+1} \delta_{rc} \sum_{l=0}^{k-j-1} \binom{k-j-1}{l} (-1)^{l} \left( \frac{\delta_{cr}}{\delta_{cr} + (N-j-l)\mu^c} \right) \]

\[ 2 \leq r \leq N \]

With this probability distribution of the tumor size in both the states, we can analyze the tumor behavior by obtaining the characteristics of the model. The probability that there are no cancer cells in the tumor when the radiotherapy is under administration is
\[ P_{c,0} = \sum_{k=0}^{N-1} \left( \frac{N}{N-k-1} \right) \delta_{sr} K_k \sum_{i=0}^{N-k} \left( -1 \right)^{N-k+i} \frac{1}{\delta_{sr} + (N - k - i)\mu^i} \]

\[ + \delta_{sr} K_m f \left( P_{r,N} \right) \quad (57) \]

Similarly the probability that there are no cancer cells in the tumor when the patient is in recovery state is

\[ P_{r,0} = (A_N K_{N-1} - B_N K_{N-2} - D_N) P_{r,N} \quad (58) \]

Where \( P_{r,N} \) and \( K_N \) are as given in the equations (57) and (37).

The average number of cancer cells in the tumor is

\[ L = \sum_{n=0}^{N} n P_{r,n} + \sum_{n=0}^{N} n P_{c,n} \quad (59) \]

The variance of number of cancer cells in the tumor is

\[ V = \sum_{n=0}^{N} n^2 P_{r,n} + \sum_{n=0}^{N} n^2 P_{c,n} - L^2 \]

Where \( L \) is as given in the equation (59).

### Table

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<th>( \delta_{cr} )</th>
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6 CONCLUSION:
For various values of the parameters $N, \delta_{rc}, \delta_{cr}, \mu^r, \mu^c, \lambda$. The values of average number of cells in the tumor and Variability of the number of cells, the probability of that there are no cancer cells in the tumor when the patient is under Radiotherapy and in recovery states $(P_{r0} and P_{c0})$ are computed and given in the Table. From the equations 57 to 60, and the table, it is observed that $P_{r0} and P_{c0}$ are decreasing when $\lambda$ is increased for fixed values of $\mu^r, \mu^c$ and $N$. As $N$ increases, the $P_{r0} and P_{c0}$ are decreasing when other parameters remain fixed. It is also further observed that the Variance of the number malignant cells in tumor is a decreasing function of $\mu^r, \mu^c$ when the other parameters are fixed.

7 REFERENCE: