2.1 INTRODUCTION

Based on the evolution and the processes involved for dose calculation, the radiation dose estimation algorithms are classified into three major groups as shown in Figure 2.1.

- Correction-based
- Model-based
- Principle-based

Figure 2.1 Life Cycle of Photon Dose Calculation Algorithms
2.2 CORRECTION-BASED ALGORITHMS

2.2.1 RADIATION DOSE TREATMENT PARAMETERS

In external beam dose delivery with incident beams as photon, the main treatment parameters are illustrated as shown in the Figure 2.2.

- **Z** is depth of treatment
- **A** is field size
- **SSD** is Source-Skin Distance in SSD setups
- **SAD** is Source-Axis Distance in SAD setups.

The others parameters are photon beam energy, number of beams used in dose delivery to the patients, treatment time and number of monitor units (MUs) for linacs.

**Figure 2.2 Parameters for Correction Based Algorithms**
2.2.2 EQUIVALENT COLLIMATOR FIELD SIZE

The rectangular aperture of the Multi-Leaf Collimator is equivalent to square aperture as shown in Figure 2.3 and is determined by the following expression as shown in equation 2.1.

\[ a_{equi} = \frac{2ab}{a+b} \]  

\[ (2.1) \]

![Figure 2.3 Equivalent Collimator Field Size](image)

Correction based algorithm is a type of empirical dose calculation which estimates dose from few basic measurements in water such as

2.2.2 PERCENTAGE DEPTH DOSE

Consider \( D_a \) as the dose delivered to the small mass of tissue at depth within patient and let \( D_0 \) be the dose delivered to the same mass of tissue at a depth \( d_{max} \) fixing the Source to Skin Distance (SSD) constant as shown in Figure 2.4. Then PDD is defined as shown in equation (2.2).

\[ PDD(Z, A, f, hv) = 100 \frac{D_Q}{D_p} \]

\[ (2.2) \]

Where, \( D_Q \) is the dose at arbitrary point Q at depth Z on beam central axis.

\( D_p \) is the dose at reference point P at depth \( Z_{max} \) on beam central axis.
2.2.3 SINGLE PENCIL BEAM CONVOLUTION ALGORITHM

This algorithm takes into account for homogeneous medium only and heterogeneities in the medium is not modeled as shown in equation 2.3.

\[
D(x, y, z) = \frac{(f + z_{\text{ref}})^2}{(f + z)^2} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} F(x', y')P_{\text{in}}(x', y', z)K(x - x', y - y', z)dx'dy' \tag{2.3}
\]

Where, \( f \) being Source-to-Surface Distance (SSD)

\( z \) being depth of dose calculation

\( z_{\text{ref}} \) being reference depth

\( F(x', y') \) being photon fluence

\( P_{\text{in}}(x', y', z) \) being primary beam off-axis intensity profile which accounts for the presence of the flattening filter.
\( K(x - x', y - y', z) \) being depth dependent Pencil Beam Kernal (PBK).

The patient is assumed equivalent to water for the algorithm of pencil beam dose calculation. Hence correction factors are applied for the inhomogeneity due to presence of lungs, bones in the patient. The inhomogeneity correction methods are generally classified into two types

- Tissue-Air Ratio Method
- Modified Batho Method

2.2.3 TISSUE-AIR RATIO METHOD

This is based on the attenuation law, taking into account the following two parameters as follows

- The depth of the calculation point.
- The field size into account.

The comparison of differences in dose at a point to attenuation and suffering of the beam in a phantom with dose at same point in air is modelled as shown in equation 2.4.

\[
TAR(d, A, E) = \frac{D_{\text{water}}(d, SAD, A, E)}{D_{\text{air}}(SAD, A, E)}
\] (2.4)

Where, \( D_{\text{water}} \) being dose in water and \( D_{\text{air}} \) being dose in air as in Figure 2.5

\( d \) being depth in water

\( SAD \) being source-axis distance

\( E \) being energy of the beam

\( A \) being field size projected at calculation point.
The Correction Factor for TAR at different densities for setup such as shown in Figure 2.6 and is calculated as shown in the equation 2.5.

$$C_F = \frac{TAR(d_2 + d_3, A)(\rho_3 - \rho_2)}{TAR(d_3, A)(1 - \rho_2)}$$  \hspace{1cm} (2.5)

Where, $d$ being actual depth of P from the surface

$d_{eff}$ being effective (or water equivalent) depth obtained by scaling the depth by the inhomogeneity density: $d = d_1 + \frac{\rho_2}{\rho_0} d_2 + d_3$

$A$ being field size projected at point P
2.2.5 MODIFIED BATHO METHOD

The Correction Factor by applying Modified Batho Method as shown in equation 2.6

\[ C_p = \frac{TAR(d_2 + d_1, A)^{(\rho_3 - \rho_2)}}{TAR(d_1, A)^{(1 - \rho_2)}} \]  \hspace{1cm} (2.6)

Where, \( \rho_3 \) being density in which point P lies (\( \rho_3 = \rho_T \))

\( \rho_2 \) being density of the overlying material

\( A \) being field size projected at point P

2.2.5 TISSUE PHANTOM RATIO

This is suitable for isocentric setups with megavoltage photon beam energies. Tissue Phantom Ratio (TPR) depends upon three parameters similar to TAR follows namely Z, \( A_Q \) and energy respectively.

The visualization of ratio between absorbed dose at a given depth in a Phantom to absorbed dose at the same point at a reference depth is shown in Figure 2.7.

\[ \text{Figure 2.7 Illustration of Tissue Phantom Ratio} \]
2.3 MODEL BASED ALGORITHMS

2.3.1 TERMA and KERNEL

The Total Energy Released in a Medium is known as TERMA. Considering the position \( r^* \) as the energy irradiated by the primary photon in the medium, the amount of energy deposited is given by TERMA \((r^*)\). The KERNEL is energy deposited about the primary interaction site.

The fraction of energy accumulated at point \( r \) from the energy released from the position \( r^* \) is given by Kernel \( K(r - r^*) \). The incident primary photons deliver TERMA to the interaction medium. The secondary electrons, that acquires this energy and travel away from the position where initial energy has been released. As they migrate they deposit energy along the track.

Kernel \( K(r - r^*) \) is location specific function, that changes at every position in patient. It portrays dose calculation resolution as well as its voxel range. In other words, it acquires the element of one set and operates a function to map them onto some other set. This result in a graph of fractional energy accumulated in various radial shells along the grid.

The process of TERMA calculation based on three beam source model is

Step 1: The fluence at each voxel is calculated with binary MLC plane with hit and miss test as shown in Figure 2.8.

![Figure 2.8 Binary Plane Multi-Leaf Collimator](image)
Let primary photon source from the Gantry head of IMRT be denoted as point source $C_p$. Then the primary photon source equation is as shown in equation 2.7.

$$src_{pri}(r) = C_p \tag{2.7}$$

The next state is scattered photon source from primary collimator known as Annulus shape and is as shown in equation 2.8.

$$src_{shp}(r) = C_{shp} \tag{2.8}$$

The last state of scattered photon source from other structures such as disk shape and intensity function with respect to $r$ is as shown in equation 2.9.

$$src_{shp}(r) = \frac{A_s}{r} \exp(-k \bullet r) \tag{2.9}$$

Step 2: The calculation of beam divergence is shown as in equation 2.10.

Figure 2.9 Illustration of Beam Divergence
The Visualization of beam divergence is shown in Figure 2.9.

\[
Fluence_{\text{div}} = Fluence_{\text{init}} \cdot \left( \frac{\text{dis}_{\text{ref}} (= 100 cm)}{\text{SPD}} \right)^2 \tag{2.10}
\]

Step 3: Now the calculation of Horn effect is performed by the equation 2.11.

\[
Fluence_{\text{horn}} = Fluence_{\text{div}} \cdot \left( \frac{\text{hornF}(OAD)}{100} \cdot OAD \right) \tag{2.11}
\]

Step 4: Here the effective depth for each voxel is computed as shown in equation 2.12 and 2.13. The Computation of effective depth calculation of two different medium is shown in Figure 2.10.

\[
d_{\text{eff}} = \int_{r_{\text{source}}}^{r_{\text{vol}}} \rho(r) dr \tag{2.12}
\]

\[
d_{\text{eff}} = \sum_{r_j=\text{source}}^{r_{\text{vol}}} \rho(r_j) \Delta r \tag{2.13}
\]
Step 5: The calculation of beam softening effect results in uniform distribution of photon beam as shown in Figure 2.11 and is expressed as in the equation 2.14.

![Illustration of Beam Softening Effect](image)

**Figure 2.11** Illustration of Beam Softening Effect

\[
d_{\text{soften}}(OAD) = \frac{1}{1 - f_{\text{softening ratio}} \cdot OAD} \cdot d_{\text{eff}}
\]  

(2.14)

Step 6: The Final state to estimate TERMA distribution in a medium is to calculate attenuation as in equation 2.15 and 2.16.

\[
TERMA_{\text{mono}}(E) = \text{Fluence}_{\text{mono}} \cdot \exp \left( -\frac{\mu}{\rho}(E) \cdot d_{\text{soften}} \right) \cdot E \cdot \frac{\mu}{\rho}(E)
\]  

(2.15)

\[
TERMA = \sum_{E_{\text{min}}}^{E_{\text{max}}} TERMA_{\text{mono}}(E)
\]  

(2.16)
2.3.2 COLLAPSED CONE CONVOLUTION

The integral that describes amount of overlap that a function has on another is known as convolution and is as shown in Figure 2.12. The calculated dose is convolution of

\[ Dose = \text{TERMA} \otimes \text{Kernel} . \]

The radiation dose is calculated from the TERMA and the Kernel as shown in equation 2.17.

\[
D(\vec{r}) = \int T_p(\vec{r}^*) \cdot \text{Kernel}(\vec{r} - \vec{r}^*) \, d^3\vec{r}^* \tag{2.17}
\]

**Figure 2.12** Visualization of Convolution

The convolution processes with same Kernel everywhere, whereas the superposition processes with a spatially dependent kernel. The kernel is framed based on density. The energy released due to incident primary photon in lung can move farther than the same energy released on tissue. Therefore superposition models reality closely than convolution. With the replacement of all distance parameters in convolution equation by radiological distance through the relation \( \rho = \rho_r^* \), superposition equations are obtained. This modification can handle heterogeneities, suitable to compete with Mote Carlo having a slight difference in terms of accuracy.

The secondary electron transport is not considered in Pencil Beam Convolution. This is the main difference between Pencil Beam Convolution and Collapsed Cone Convolution algorithm (CCC). The CCC algorithm tries to maintain a trade-off
between accuracy of Convolution/Superposition (CS) and speeding up the computation. The CCC algorithm uses spherical coordinates \((r, \theta, \phi)\) instead of Cartesian coordinates \((x, y, z)\).

The Pseudo code for process of Convolution is written as follows.

Generate Poyenrgetic_Spherical_Kernel \((r, \theta, \phi)\)

Create Accumulative_Kernel \((r, \theta, \phi)\)

For (All 3D voxels with \((Xp, Yp, Zp)\) )

{  
  For (All \(r, \theta, \phi\))
  {
    Calculate_vector()
    Get_transformed_voxel_Lists()
    Calculate effective_pathlength(voxel_Lists)
    For (All Listed voxels)
    {
      Calculate \(\theta_{\text{deviation}}\)
      Energy = Accumulative_Kernel\((r_{\text{in}})\) - Accumulative_Kernel\((r_{\text{out}})\)
      Get_TERMA(Voxel)
      Dose +=Energy * TERMA
    }
  }
}

}
2.3.3 MONTE CARLO METHOD

The dose deposition is calculated by tracing the histories of millions incident photon and secondary electrons that involve in interaction with matter based on physics. This method has high precision for dose calculation but takes long computation time. To determine the path of incident photon a number between 0 and 1 is selected using random number generators.

Due to photon interaction the events that are of importance in Monte Carlo are

2.3.3.1 PHOTOELECTRIC EFFECT

When a bounded electron from the shell of an atom is ejected, by the interaction of incident photon beams, it results in a phenomenon known as Photoelectric effect. The visualization of photoelectric function is shown in Figure 2.13

\[ E_{\text{ph}} = h\nu - BE \]

Figure 2.13 Photoelectric Effect

The expression for photoelectric effect is as shown in equation 2.18

\[ E_{\text{ph}} = h\nu - BE \] (2.18)
Where \( h\nu \) is energy of incoming photon and BE is binding energy of the atomic shell from which the electron is ejected out. The atom now in an excitation state releases characteristic radiation and Auger electrons to settle in ground state as shown in Figure 2.14

![Figure 2.14 Characteristic of Radiation Emission and Energy carrier Auger Electron](image)

### 2.3.3.2 COMPTON EFFECT

When an incident photon on interaction with loosely bound electron or free electron gets scattered with reduced energy by transfer of some energy to electron is known as Compton Effect as shown in Figure 2.15. The expression for energy transferred to the electron is as shown in equation 2.19.

\[
E_{\text{c}} = h\nu - h\nu^* \tag{2.19}
\]

Where \( h\nu \) being the incident photon’s energy and \( h\nu^* \) the scattered photon’s energy.
2.3.3.3 PAIR PRODUCTION

When an interaction occurs among the electromagnetic field of atomic nucleus electron and positron pair is created and this phenomenon is known as Pair Production as shown in Figure 2.16. The critical energy level for pair production phenomenon to occur is $2m_e c^{2.0} = 1.0222 Mev$. For energies above this critical value with respect to $\hbar \nu$ the mass attenuation coefficient $\frac{k}{\rho}$ increases swiftly and directly proportional to atomic number $Z$. This effect is known as triplet production when the incoming photon interacts with the field of orbiting electron as shown in the Figure 2.16. The critical energy level for triplet production is $4m_e c^{2.0}$.

All these events lead to electron interactions which induce ionization, excitation, and bremsstrahlung thereby resulting in dose deposition.
2.4 PRINCIPLE BASED ALGORITHM

2.4.1 RADIOBIOLOGY

The act of ionizing radiation on living organisms is investigated in radio biology. This action is very complex involving multidisciplinary concepts like

- Various types of ionizing radiation

- The energy absorption due to incident radiation with matter at atomic and molecular size leads to biological damage.

- The repair mechanism involved to overcome damage in living organisms from physics, chemistry and biology respectively.
These basic mechanisms are utilized in radiotherapy to kill tumor shielding the normal tissues as far as possible. The various phrases of radio biological damage as shown in Figure 2.17

![Figure 2.17 Phases of Radiobiological Damage](image)

The biological systems are too much sensitive to the incident radiation. There is a rise of temperature in water for approximately 10-3 °C due to incident photon dose of 4Gy. This is equivalent to around 67 calories in 70 kg human being. If the same dose is delivered to whole body of human is lethal in 50% of cases [LD50].

2.4.2 TYPES OF IONIZING RADIATION

Generally ionizing radiations do possess energy to knock an electron from an atom. Alpha, beta, photon [X-ray and gamma rays] and neutron are four main types of ionizing radiation. These radiations can penetrate the human body at varying depth to deliver radiation dose as shown in Figure 2.18.
Alpha radiation is the particles formed by two protons and two neutrons which have double positive charge. Since they have relative heavy mass and charge, their ability to penetrate matter is extremely limited and can be stopped by a piece of paper.

The charged particles that are generated from atom’s nucleus are beta radiation. This negatively charged beta particle can penetrate very deeply than alpha particle as they are very small. They can deposit their energy within the active skin cell of human body.

Photon is an electromagnetic radiation. Two types of photon radiation those are familiar in dosimetry is X-rays and gamma rays. The photons that emit from nucleus are gamma ray, whereas the photons that generate from outside of nucleus are X-ray. Photons can penetrate organs and tissues of human body.

Neutron originates from the process of spontaneous fission which further bombards the adjacent atom to produce further fission resulting in a chain reaction. This principle is applied in nuclear reactor to generate power.
2.4.3 LINEAR ENERGY TRANSFER

The physical quantity that addresses the quality of ionizing radiation beam is Linear Energy Transfer (LET). It is defined as the ratio of mean dE energy imparted locally to the medium by the charged particle of specific energy in traversing a distance of dl. The unit of LET is Kev/µm and its values for various radiation source is shown in Table 2.1.

<table>
<thead>
<tr>
<th>Radiation Source</th>
<th>Values in keV/µm</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 kVp x ray</td>
<td>2</td>
</tr>
<tr>
<td>Cobalt-60 gamma ray</td>
<td>0.3</td>
</tr>
<tr>
<td>3 MeV x ray</td>
<td>0.3</td>
</tr>
<tr>
<td>1 MeV electron</td>
<td>0.25</td>
</tr>
</tbody>
</table>

2.4.4 RELATIVE BIOLOGICAL EFFECTIVENESS

This facilitates for comparison of test radiation with a benchmarked radiation. It is the ratio of dose among the two radiations to provide certain biological effect. Benchmarked radiation is either X-rays of 250Kev or \(^{60}\)Co gamma rays of 1.33Mev. RBE is written as

\[
RBE = \frac{\text{BENCHMARK RADIATION}}{\text{TEST RADIATION}} \text{ for a given effect}
\]

The biological effect estimation is based on cell killing or cell transformation. The ingredients of cell are organic compounds and inorganic compounds made of proteins, lipids, carbohydrates, nucleic acids and water along with minerals respectively. Cytoplasm and nucleus are two main components of cell, that supports all metabolic functions inside the cell and which possesses genetic information (DNA) respectively.
The main target of ionizing radiation is DNA molecule prone to breakage in chemical bonds. Based on the extent of damage several repair mechanism are available for recovery in living organisms. The operation of recovery mechanism is classified into three categories

- Lethal Damage (LD) to cells is irreversible where recovery mechanism is impossible which ultimately leads to cell death.
- Potentially Lethal Damage (PLD) to cells can be recovered from radiation damage by post irradiation environmental conditions.
- Sub Lethal Damage (SLD) to cells can be recovered in hours under normal conditions provided that second fraction of dose is not delivered.

2.4.5 DNA STRUCTURE

The Figure 2.19 shows the structure of DNA molecule having many deoxyribo nucleotides (bases) tied in a chain like arrangement. The bases supported by hydrogen bonds are paired complementary such as adenine with thymine and cytosine with guanine. The structure is symmetrical to reconstruct the other half. The DNA molecule is made of two anti-parallel helices twisted in a form of ladder. During the process of cell division every strand in DNA is self-replicated which leads to formation of identical molecules.

When exposed to external radiation DNA strand undergoes either single or double strand breakage. Single strand breakages are reconstructed by the opposite strand as template. Whereas the interaction of DNA having two double strands break leads to cell killing, mutation or carcinogenesis. The genetic abnormalities in germ cells due to mutation can be inherited by offspring. The same effect in somatic cells can induce diseases including cancer which called carcinogenesis.

Generally human cells are somatic and germ cells. When a new cells are formed through division. The division of somatic cells is known as mitosis and germ cell is known as meiosis.
2.2.6 METHODS OF CELL DAMAGE

The causes of DNA damage are by two ways of ionizing radiation.

- Direct action of radiation with secondary electron generated from absorption of X-rays photon interacts with DNA molecule to produce an effect.

- Indirect action where secondary electron interacts with water molecule to form a hydroxyl radical (OH-) that in turn creates damage to a DNA.

As 80% of cell constitutes water, the interaction of incident photon with water molecule leads to ionization as shown in equation 2.20

\[ H_2O \rightarrow H_2O^* + e^- \]  \hspace{1cm} (2.20)
The $H_2O^{**}$ being an ion radical having a lifetime of approximately 10-10 s, decays to form intensively reactive hydroxyl free radical $OH^\bullet$ as shown in equation 2.21

$$H_2O^{**} + H_2O \rightarrow H_3O^+ + OH^\bullet$$  \hspace{1cm} (2.21)

Generally two out of three incident X-ray create damage to DNA of human cell are caused by hydroxyl, which approximately has a lifetime of 10-3 s.

### 2.2.7 THE CELL CYCLE

The cell proliferation cycle is addressed by two familiar time periods

- Mitosis M where cell division occurs and
- S- the period of DNA synthesis

There two gaps between M and S, namely G1 and G2 respectively. G1 is the first gap in activity in between mitosis and S phase. G2 is the second gap in activity between S phase and the consequent mitosis. G0 denotes cell cycle arrest as shown in Figure 2.20 when the cell stops progressing along the cycle. The cells are highly radiosensitive in M and G2 phases and can withstand in late S phase.

![Figure 2.20 The Cell Cycle](image)

34
The causes of cell death are due to non-proliferating cells those losses specific function and stem cells that loose reproductive integrity. A colon genic is a surviving cell that proliferates independently by maintaining its reproductive integrity.

2.2.8 CELL SURVIVAL AND LINEAR QUADRATIC EQUATION

The most promising method of fitting the survival of cells after incident ionizing radiation is as shown in equation 2.22

\[ S = \frac{N}{N_0} = e^{-\alpha D - \beta D^2} \]  \hspace{1cm} (2.22)

Where, \( S \) is the surviving cells count after a dose of \( D \)

\( \alpha \) and \( \beta \) denotes the linear and quadratic components of the survival curve.

Since \( \alpha \) term associates with the linear curve, the cell death as a result of \( \alpha \) component increases with linear dose. Similarly \( \beta \) term associates with the quadratic curve, the cell death as a result of \( \beta \) component increases in proportion of square of dose.

The ratio of \( \alpha \) and \( \beta \) is computed for the dose \( D \) in equation 2.23 by equating the linear and quadratic term of equation 2.23.

\[ \alpha D = \beta D^2 \ \text{or} \ D = \frac{\alpha}{\beta} \]  \hspace{1cm} (2.23)

The higher ratio for tissues when plotted on logarithmic scale tends to show a more linear slope. Tissues with low ratio have a parabolic shape.

Based on LQ model with total dose \( D \), fraction dose \( d \) and tissue dependent ratio \( \frac{\alpha}{\beta} \) as parameter the Biological Effective Dose (BED) is shown as in equation 2.24.
\[ \text{BED} = D \left[ 1 + \frac{d}{\alpha / \beta} \right] \]  

(2.24)

Consider two varying fractionation schemes with D2 being the total dose for the new fraction dose d2 that relates to the total dose D1 from the benchmarked fraction dose d1 will be calculated by solving the equation 2.25 for desired measure

\[ \frac{D_2}{D_1} = \frac{d_1 + (\alpha / \beta)}{d_2 + (\alpha / \beta)} \]  

(2.25)

In case of dose fraction = 2Gy, then Biologically Equivalent Dose (BED) is given as in equation 2.26

\[ \text{EQD}_2 = D_1 \cdot \frac{d_1 + (\alpha / \beta)}{2 + (\alpha / \beta)} = \frac{\text{BED}}{1 + \frac{2}{\alpha / \beta}} \]  

(2.26)

Based on LQ model the biological equivalent treatment is calculated with the expression as shown in equation 2.27

\[ \alpha D + \beta qD^2 - \frac{t}{T_{pot}} = \alpha_1 D_1 + \beta_1 q_1 D_1^2 - \frac{t_1}{T_{pot}} \]  

(2.27)

Where, the dose rate function accounts for sub lesion damage repair that occurs between events q(t).

\( T_{pot} \), is potential doubling time parameter that characterizes cell kinetics.

2.2.9 TUMOUR CONTROL PROBABILITY

TCP model depends on the assumption that tumour control requires the destroying of all tumour tissues. The probability of this occurrence is predicted by Poisson statistics as shown in equation 2.28

\[ \text{TCP} = \exp[-N \cdot P_r(D)] \]  

(2.28)

Where, N is number of tumour tissues in initial state.
\( P_s(D) \), is the probability of cell survival fraction after an application of dose D.

By considering that cell survival can be addressed by linear and quadratic terms, then the equation 2.29 can be written as

\[
P_s(D) = \exp(-\alpha D - \beta D^2)
\]  (2.29)

With additional two parameters that characterize the dose and normalized slope at the position of 50% probability of control, \((D_{50}, \gamma)\), the equation 2.30 can be written as

\[
TCP = \left(\frac{1}{2}\right) \sum_{i} \exp\left(\frac{2\pi i}{\ln(2)} \left( \frac{D_{i}}{D_{50}} \right) \right)
\]  (2.30)

The other TCP models familiar in literature are

- The Martel Model is as shown in equation 2.31.

\[
TCP(D) = \frac{1}{1 + \left( \frac{D}{D_{50}} \right)^\gamma}
\]  (2.31)

Where, \(D_{i}, D_{50}, \gamma\) is dose administered to the fractional volume \(v_{i}\), the dose required to satisfy 50% probability of tumour control, the sigmoid shaped normalized slope of dose response curve at the position 50% probability control respectively.

- The Fenwick model in TCP estimation is as shown in equation 2.32

\[
TCP(D,V) = \Phi \left\{ \frac{D - D_{50} - C \left[ \ln(V) - 5 \right]}{mD} \right\}
\]  (2.32)

Where \(m, C\) are constants and \(\Phi\) is the Gaussian integral

- The Webb Nahum model is as shown in equation 2.33
The Nitin model is as shown in equation 2.34

\[
TCP(D) = \sum_{j=1}^{k} \frac{1}{\sigma \sqrt{2\pi}} e^{-\frac{(D_j - a_j)^2}{2\sigma^2}} \exp\left(-\rho \exp\left(-a_j\rho\right)\right)
\]  

(2.34)

Where BED calculated by the Linear Quadratic (LQ) model and L is maximum tumour diameter.

2.2.10 NTCP MODEL

This critical component model relies on the assumptions that

- An organ is composed of number of identical components
- The response of one component does not correlate with that of any other
- A complication is reported when one or more components non-proliferated, that is every component of the organ is critical.

Such components can be marked with the functional subunit (FSU).

Consider that the organ consist of N such critical components and the probability of injury to a single FSU is equal to \( p \). For a given kind of tissue and fractionation scheme, the probability \( p \) is only a function of irradiated dose \( D_j \) delivered to the jth FSU. The probability \( P^* \) that jth FSU escapes injury is then \( 1 - p(D_j) \) and by Binomial statistics for uncorrelated events, the complication probability for overall organ is as in equation 2.35

\[
P^* = 1 - p(D_j)
\]

(2.35)

Now with the product taken over the each of the FSU the probability of complication for entire organ is as given in equation 2.36
The other familiar NTCP models from literature are

- **The LKB model** is as shown in equation 2.37

\[
NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} e^{-\frac{1}{2}x^2} dx, \quad mEUD = \left[ \sum_{j=1}^{n} V_j D_j^{\alpha} \right]^{\frac{1}{\alpha}}
\]

Where is the uniform dose irradiated to the small volume with other variables n, m and TD50 being constants

- **The Fenwick model of NTCP calculation** is as shown in equation 2.38

\[
NTCP = \Phi \left( \frac{D - 29.2}{13.1} \right)
\]

Where, D the mean organ dose and the normal distribution

- **The mEUD model** is as shown in equation 2.39

\[
mEUD = \left\{ \sum_{j=1}^{n} V_j D_j^{\alpha} \left( 1 + \frac{d_j}{\alpha/\beta} \right) \right\}^{\frac{1}{\alpha}}
\]

Where N is the count of total dose bins.