# SRI VENKATESWARA INTERNSHIP PROGRAM FOR RESEARCH IN ACADEMICS (SRI-VIPRA)

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## "Dose Calculation Algorithms and associated Range Uncertainties in Proton Beam Radiotherapy"

**IQAC**
**Sri Venkateswara College**
**University of Delhi**
**Dhaula Kuan**
**New Delhi -1100**

# SRIVIPRA PROJECT 2022

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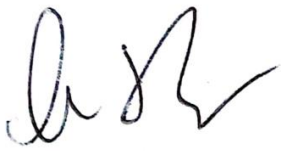
|---|---|
| **Name of Mentor:** Prof. Anant Pandey<br>**Name of Department:** Department of Physics<br>**Designation:** Professor | **Photo**<br>  |

## Title: Dose Calculation Algorithms and associated Range Uncertainties in Proton Beam Radiotherapy

List of students under the SRIVIPRA Project:

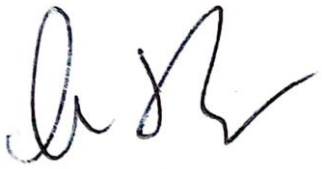
| S.No | Name of the student | Course | Photo |
|---|---|---|---|
| 1 | Pallavi Agrawal | BSc. (Hons.) Physics |  |
| 2 | Surabhi Srivastava | BSc. (Hons.) Physics |  |



**Signature of Mentor**

# Certificate

This is to certify that the aforementioned students from Sri Venkateswara College have participated in the summer project SVP-2238 titled "**Dose Calculation Algorithms and associated Range Uncertainties in Proton Beam Radiotherapy".** The participants have carried out the research project work under my guidance and supervision from 21st June 2022 to 25th September 2022. The work carried out is original and carried out in an online mode.



**Signature of Mentor**

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## ABSTRACT

The distinct property of protons to deposit a high dose at a specific depth in the media, called the range, differentiates it from traditional means of radiotherapy. This property is understood by studying proton interactions in medium. To realize the use of proton radiation in treatment of tumors, several factors have to be considered and adjusted to calculate precise doses for treatment plans. A proper distribution of proton energies has to be determined such that the dose being deposited covers the volume of tumor efficiently. Moreover, the heterogeneities in the path of incident proton beams have to be attuned in treatment plans to ensure proper dose deposition at range under consideration. The straying of protons from incident path due to non-elastic scatters which contribute to inherent beam spread have to be well included in dose calculations. Two major classes of dose calculations widely used in proton beam radiotherapy, pencil beam algorithm and Monte Carlo simulation have been intensely studied and the inference is presented in this review paper along with factors that have to be deliberately considered to plan an efficient and custom dose plan for a patient via both dose calculation approaches. At various stages such as imaging, setup, beam delivery and dose calculations, the presence of range uncertainties largely limit the ease of implementation of proton radiotherapy. Range uncertainties particularly due to dose calculation method are discoursed in this paper along with a few techniques to minimize their effects.

Keywords: multiple coulomb scattering, hard scatters, proton range, stopping power, Bragg peak, SOBP, range straggling, dose calculations, pencil beam algorithm, beam spread, Monte Carlo simulation, heterogeneities, range uncertainties

## INTRODUCTION

Proton beam radiation therapy centres are emerging around the world with specific treatment plans and beam shaping technologies. The properties of protons differ impressively from that of photons which poses a huge advantage in their usage in radiation therapy. The chief objective of radiotherapy is to maximize effects of radiation on tumour cells while keeping the damage done to healthy cells at a minimum. Therefore, studies predominantly focus on two aspects: developing new treatment planning systems to deliver higher doses of radiation to defined target volumes and searching for new forms of radiation therapy to improve the therapeutic ratio. The fact that proton beams can theoretically produce excellent dose localization is described in the paper. Hence, dose escalation can be easily performed while mitigating radiation toxicity in surrounding normal tissues. Most importantly, to come up with an efficient treatment plan which is patient specific, it is fundamentally important to study the modes of dose calculation and choose the most efficient approach amongst others for a particular treatment case.

Although proton beam radiotherapy is a quite advantageous mode of treating cancers, it encounters various challenges. As the tissues in the body are inhomogeneous and every organ is made up of different kind of tissue, it introduces complications in modelling the right plan of dose deposition and determining the energy of proton beam the patient will be subjected to. The motivation behind this review paper is to understand the process of

dose deposition via protons and study the limiting factors introduced in dose calculation algorithms and sequentially, in range uncertainties, due to properties of protons and their interactions with media. This review paper intensely focuses on the two most prominent dose calculation modes being used in proton beam radiotherapy centres namely, pencil beam algorithm and Monte Carlo simulations. Dose delivery methods are an important factor that affect the way dose deposition calculations are determined in the medium and these points are strikingly explained through this paper. Both intrinsic and extrinsic factors have to be closely studied to obtain a complete picture of the dose calculation algorithms.

The reader is encouraged to appreciate the advantageous aspect of proton beam radiotherapy without turning a blind eye to the challenges in the path of reaching its full potential. Active research is in progress to determine the efficiency of proton beam radiotherapy over the traditional mode of using photons. The future of using proton beams in radiotherapy seems to be very promising but it can only become a reality if the existing hurdles can be overridden such as minimizing range uncertainties and speeding up dose calculation without significant trade off in precision.

## PROTON BEAM RADIOTHERAPY

Protons are charged particles that possess mass whereas photons are charge less and massless particles. This brings out a major difference in the way the two kinds of particles interact with the atoms in a medium. Neutral charges are indirectly ionizing. Photons, being neutral particles, don't deposit energy directly in matter. They first lose their energies to charged particles which in turn deposit energy to matter. Due to this, not all their energy gets deposited locally to the targeted tissue. Photons lose energy via processes of Compton scattering, Pair Production, Photo-electric effect and Bremsstrahlung effect depending on the energies they carry and the nature of particles in matter they are interacting with (nucleus/electrons). They lose most of their energy at the surface and rate of energy release per unit length inside the medium attenuates exponentially as it propagates through it. Due to this reason, a huge fraction of distil dose is deposited in the healthy tissues. This intrinsic characteristic of photons cannot be interfered with. The best that can be done to maximize damage done to the tumour cells is to irradiate the target from multiple directions such that the cumulative dose from all incident beams is highest in the region of tumour cells and the energy deposited is enough to efficiently eliminate tumorous cells. But this technique produces a larger low-dose irradiated volume of normal tissues around the target. In proton beam radiotherapy, this problem is overcome to a large extent as a very small fraction of energy is released to the medium initially until incident protons reach a relatively well-defined penetration depth where they deposit most of their energy and come to a stop. The penetration depth is adjusted to coincide with the tumour depth in the patient's body which results in maximum damage done to the tumour cells.

The unique properties of a proton particle, notably the mass that it possesses, make its Bragg curve much more spiked than that of an X-ray or a gamma ray particle**.** It also makes the trajectory of a proton much easier to control. The proton beam has relatively

sharp edges with little dose deposited laterally due to side scatter. As such entrance dosages are considerably reduced in proton therapy as compared to X-ray or gamma ray radiation and exit dosages are almost completely eliminated which are the major concern in case of X-ray or gamma ray radiation especially in the treatment of tumours adjacent to critical organs. The sparing of nearby normal tissues from irradiation reduces side effects of treatment and reduces the risk of developing secondary malignancies.

Protons interact with the constituent particles in the medium via the following three physical processes, which determine the dose distribution of a beam.[3]

1) Stopping: A major fraction of the penetrating protons lose energy and eventually come to a halt by repeated electromagnetic (EM) interactions with atomic electrons, and to a smaller extent with atomic nuclei. The only force being involved is the EM force.
2) Multiple Coulomb scattering (MCS): The protons get deflected from their original path by EM collisions with atomic nuclei, and to a smaller degree by atomic electrons. The angular deflection caused by a single collision is very small and the net deflection is a result of several single scattering events combined. Therefore, scattering is referred to as multiple columbic scattering. Here also, EM force is the only force in play.
3) Hard scatters: A very few protons (estimated to be only 20% at proton therapy energies) go through single hard scatters either with the nucleus as a whole or with its constituents. This process may involve the strong nuclear force or the EM force.

Particles emerging from a hard scatter (which can be an elastic, an inelastic or a non-elastic collision) are called *secondaries* and includes the incident proton, other protons, neutrons and particle clusters that are knocked out of the nucleus due to the collision, and the residual nucleus itself. The particles that stop without going through a hard scatter are called *primaries*. Sometimes, elastically scattered protons are called primaries.

Since hard scatters are rather infrequent, we do not need to consider them in most proton therapy design and treatment problems. In problems like dose calculation where high accuracy is a priority, the effect of hard scatters is accommodated as a correction in case of analytical methods and by using empirical data or nuclear models in case of computational techniques. The MCS theory predicts that the angular distribution of scattered protons, in a plane perpendicular to the axis denoting the depth of penetration, is Gaussian in nature with a tail that attenuates far more slowly. But since the Gaussian core consists of 99% of these protons, the transverse spread can be modelled by Gaussian distribution. It is a good approximation that provides us with results within the required accuracy range and we will be using this Gaussian approximation in the dose calculation algorithms later in this paper. Stopping is explained by the simple and well-established theory of Bethe-Bloch, which is discussed in the following section.

**Stopping potential**

Stopping potential is the measure of energy loss per unit length of charged particles traversing matter. The Bethe formula for non-relativistic particles is given as below

$$-\frac{dT}{dx} = \left(\frac{4\pi N z^2 Z e^4}{m_e v^2}\right) \ln\left(\frac{m_e v^2}{\bar{I}}\right)$$

Equation 1

The terms in the Bethe formula are as follows:
$N$ = number density (number of atoms per unit volume in the path of charged particle)
Z = charge per atom in the media
z = charge per charged particle
$m_e$ = mass of and electron
e = charge of an electron
v = velocity of charged particle
$\bar{I}$ = ionization factor

The term in the left-hand side of the equation is the stopping potential. The negative sign indicates that energy is lost as the charged particles propagate through the medium. Heavier the element of material is, lesser will be its stopping power.

The stopping potential is independent of the mass of ion as the force experienced by it in the medium is due to columbic interactions with electrons in the medium. The interaction between the ion and each electron in its range depends on the charge on the ion (and electron) whereas the density of atoms in the medium relates the number of atoms seen by the ion in its path. The $m_e v^2$ factor in the expression can be related to energy of proton, T (1/2 factor is omitted for ease).

**Range**

Range is defined as the depth penetrated by the proton in the target medium before it comes to a stop after losing all of its energy. The finite range of a proton trajectory in the medium is one of its most important characteristics.

The theoretical range of primaries can be calculated by obtaining the stopping power, and numerically integrating its inverse with respect to the energy. The mean projected range R of a proton with initial energy $E_i$ is given by

$$R = \int_0^{E_i} \frac{1}{S(E)}\, dE$$

Equation 2

Ideally, range would be defined at the position where the dose has decreased to 80% of the maximum dose. This is because the 80% dose fall-off position coincides with the mean projected range that is the depth at which 50% of the protons stop, making this position independent of the energy spread of the beam. This depth is also referred to as the *distal dose fall-off position*. But for historic reasons, the 90% fall-off position in water is used as the prescribed range in most proton treatment facilities.

For a given thickness of homogeneous media, the water-equivalent dose, that is the dose delivered to water with the same radiological thickness as the material media, can be calculated quite accurately if the range-energy relationship of the material in question as well as that of water is known. The accuracy depends on the precision in the range-energy relations. Keeping this is mind, we have used the SRIM software, a Monte Carlo Simulation based software, to plot functions corresponding to a 50MeV proton beam irradiating a 10cm wide medium of water molecules. For this, we chose a layer of 10mm depth made up of water molecules (2 hydrogen and 1 oxygen atom per molecule). The ions in the radiation beam are hydrogen ions with energy of 50MeV.

Protons carrying this energy enter the medium and diverge scarcely from their initial path due to MCS. A very small number of protons are scattered hugely from the incident direction by undergoing a hard scatter. The ion distribution plot gives us an insight into the dose distribution in the target [Figure 1].

Complying with the terminology used for a pencil-beam dose, we describe the three overlapping regions of dose distribution in the target. The dense central region consists of the primaries and is called the *core*. A hard scatter throws off the dose out to a large radius. The dose in the region surrounding the core consisting of the charged secondaries is the *halo*, and the *aura* is this very large region made up of the neutral secondaries. These secondary particles have different characteristics and lesser amount of energy and they deposit energy into the material away from the target site. Therefore, as the protons penetrate the medium more and more, the fluence about the central axis decreases.
From the simulation plot, we can also note that a very huge fraction of protons come to rest around 41.9 mm deep inside the medium.

Even for a mono-energetic (50MeV) incident photon beam, the graph of ion ranges shows that all the protons do not have the same fixed stopping depth rather it is spread over a thin range, 41-45 mm [Figure 2]. This fluctuation in range is called *range straggling*. It happens because EM stopping is a result of multiple discrete and random energy transfers making it a statistical process, and therefore the initially mono-energetic proton beam gains an energy spread (*energy straggling*) as it passes through the medium. It has been found that the energy distribution will be more if the incident beam also has a spread and it increases with increasing depth of penetration in the target.

The relation between energy loss and depth in target is expressed in the graph [Figure 3]. The charged proton decelerates as its energy is lost due to interactions with the atoms of the tissue, depositing a dose along its path. The rate at which it slows down increases until it reaches its peak called the *Bragg peak.* At this depth defined by the Bragg peak, which is 41–45 mm in the example case taken, the proton deposits the most amount of its energy, and then the graph is seen to be steeply dropping to zero and no energy is transferred beyond this finite range of travel. As the penetration depth of the Bragg peak depends on the initial energy of the protons, the Bragg peak can be placed precisely depending on the depth in the medium where the tumour cells lie. However, monoenergetic proton beams are not suitable for clinical use because the dimensions of most tumours are much larger than that of the narrow Bragg peak. Therefore, to cover a tumour of known shape and diameter, a distribution of proton energies is used which

creates a flat, plateau-like high dose region that effectively covers the target lesion. This is referred to as the *spread-out Bragg Peak* (SOBP), and it allows for the treatment to extend to more specific 3D shapes.

The fall-off region is the distal region of the Bragg peak where the dose drops from 80% to 20%. The width of fall-off region is due to scattering processes (MCS and Nuclear Scattering/ Hard Scatters), and statistical energy loss of individual protons that results in range straggling. When there are heterogeneities in the path of the proton beam, there is a degradation in the Bragg Peak. This results in variation of width of the fall-off region. The primary cause of Bragg peak degradation is MCS. This is supported by Urie et al (1986) in which it showed degradation in proton beams passing through the base of the skull, a highly heterogeneous region. MCS occurring at the interfaces of the heterogeneous media in the path of the proton beam is believed to be responsible for the degradation of Bragg peak.

Integral dose i.e., the total amount of energy absorbed in the body for a given target dose is always lower when using proton as compared to photon radiotherapy techniques. This is mainly due to the absence of exit dose in the former treatment. In order to fully exploit the potential advantages of proton therapy, the range of proton beams needs to be predicted as accurately as possible in the treatment planning and delivering process. The sharp gradient of the proton beam at the end of its range makes the dose distribution extremely sensitive to errors in dose calculation. Inaccuracies in the dose calculation and in the uncertainty margins quantification of proton penetration can easily shift the SOBP, which might lead to under coverage of the target and over dosage of the surrounding normal tissue. Thus, dose calculation plays a very critical role in a proton therapy treatment. Accurate and efficient dose calculation has become even more important with advancement in technology, like Intensity modulated treatment planning (IMPT) and 4D treatment planning, where repeated dose calculations are needed throughout the procedure.

## DOSE CALCULATION[4]

Dose calculation algorithms correlate treatment plans to clinical outcomes. Their main goal is to optimize treatment plans. Dose calculation runs should be able to give results quick enough to plan treatments in practical time. It also has to be precise enough to be carried out with closely determined margins. Neither high speed nor high precision can be compromised in an efficient dose calculation model. Need for highly accurate dose calculation results often lead to prolonged computation time and a balance between the two has to be maintained for a highly efficient treatment plan. This is the most crucial obstacle in dose calculation algorithms which modern developments are determined to tackle.

The accuracy of dose calculation algorithms encounters the problem of heterogeneity. A highly detailed energy transport model is required to override this problem. Development of efficient dose calculation algorithms require the knowledge of physical interactions that protons experience in media. To account for the physical interaction processes between proton beams and tissues, models relating energy transport to these physical

interactions have to be introduced. Dose kernels describe energy transport and dose deposition in water arising from a defined set of proton-tissue interactions. These dose kernels are scaled to equivalent local tissue densities to account for heterogeneities in human body. The local tissue geometries are determined via CT scans are sampled on a finer grid. These model-based algorithms give a realistic model of absorbed dose in heterogeneous media incorporating the patient's anatomy.

In this paper, we will focus on two classes of dose calculations namely, Pencil Beam algorithm and Monte Carlo simulation which are the most widely utilized methods of dose calculation in routine clinical applications and research studies.

## PENCIL BEAM ALGORITHM[4][5]

An approach to pencil beam modelling is to divide a pencil beam into smaller beam elements. The number of these elemental beams depend on the accuracy required. More subdivisions give higher precision but computation time is longer. These beam elements are weighted. The weights depend on the lateral spread of the pencil beam in air. Another approach involves total fluence calculation. Fluence is the measure of number of particles crossing an infinitesimal area, dA, normal to the beam direction. Fluence is independent of the angle of radiation. Integrating fluence over the pencil beam gives total fluence. The total fluence of the pencil beam is determined beforehand and based on it, the elemental beams are calculated that result in equal total fluence. This second method has an upper hand when it comes to computation speed, especially if the weights of elemental beams are varying after every computation step.

A mathematical beam requires several implementation considerations that has to be accounted for to approximate a physical proton beam. The primary mode of interaction out of all the modes of interactions that protons undergo in a medium is elastic scattering. The scattering events result in a Gaussian distribution lateral to the incident beam. The Gaussian distribution is a close approximation to the trailing end in reality. We aim to reach a model with zero initial lateral and angular spread. The total distribution at any point in the medium is the result of convolution of two types of Gaussian functions 1) the initial unperturbed Gaussian beam shape which is the property of incident pencil beam in air after exiting modifying devices and 2) additional spread due to multiple coulombic scattering events in the media. The spread due to MCS events are calculated using Fermi Egyes theory modified for proton beams or Highland's approximation formula. Both give parametrized formulas for the spread of proton beams in water at every point in the medium.

### Fermi Egyes Theory:

Fermi Egyes theory was firstly used for electrons but later on was modified to calculate the lateral deviation of protons from the axis of an infinitesimal, parallel proton beam at depth z in the medium. It uses an approximation that particles propagating in a medium undergo small angle scattering which is a condition that protons and heavy ions comply with well as they are heavier in comparison to electrons. The integration is along the pencil beam axis.

$$\overline{x_{MCS}^2(z)} = \int_0^z (z - z')^2 T(z') dz' \text{ (in cms)}$$

Equation 3

Here T(z') is the scattering power which is calculated using the non-local formula given by Gottenchalk. The scattering power is a function of proton momentum, $\rho$, velocity of proton v and the radiation length $L_R$.

**Highland's approximation formula:**

Highland's formula is used to calculate the lateral beam spread due to MCS in water and is preferred over the Fermi Egyes formula given above for most treatment plans. The lateral spread of protons at depth z is given as

$$\overline{x_{MCS}^2(z)} = \left[1 + \frac{1}{9}\left(log_{10}\frac{z}{L_R}\right)\right]^2 \int_0^z \frac{1}{L_R}\left[\frac{14.1MeV}{\rho v}(z - z')\right]^2 dz' \quad \text{(in cms)}$$

Equation 4

where $\rho$ is the proton momentum, v is the velocity of proton and $L_R$ is the radiation length. Product of proton momentum and velocity is known as the kinematic factor.

Beam spread for pencil beam with zero initial angular spread at z depth is given as $\overline{x_{total}^2(z)} = \overline{x_{MCS}^2(z)} + \overline{x^2(0)}$. If the initial pencil beam has a non-zero angular spread, it is taken into account by substituting $\overline{x^2(0)}$ by $\overline{x_{vaccum}^2(z)}$ which is the spread of the pencil beam in vacuum. Computation results in water are converted to that in heterogeneous medium by using water equivalent models of the heterogeneous medium taken in consideration.

Pencil beam dose calculation determines lateral spread due to MCS for every single pencil beam at each and every point in the depth so, a good calculation speed is important along with high accuracy. The limiting factor of pencil beam algorithm is the fact that it is independent of the off-axis heterogeneities present in the medium away from the beam region.

The extended tails in the spatial distribution mentioned earlier is the result of large angle scattering in the medium which leads to the dose deposition straying away a little from the central gaussian region. This dose deposition beyond the central gaussian deposition is known as the beam halo. The contribution from beam halo can be omitted for homogeneous fields but cannot be ignored in the case of non-homogeneous fields. These measurements are not easy to estimate and are sensitive to beam specifications.

The expression for dose to patient has the form:

$$D(P) = \frac{W}{2\pi\sigma^2} \exp\left(\frac{-r_P^2}{2\sigma^2}\right) D_\infty$$

Equation 5

where W is the weight assigned to a pencil beam, $\sigma$ is the total beam spread at point P ($\sigma = \overline{x_{total}^2(z)}$) and $D_\infty$ depth–dose component integrated over an infinitely broad lateral field.

Additionally, the lateral spread of a mono-energetic beam doesn't result in a clinically useful dose distribution. Moreover, in the direction of depth, a mono-energetic beam would have a sharp peak of dose deposition over negligible width inside the medium. This calls for the need of spreading the beam laterally to cover a uniform area in the lateral direction. In addition to this, Bragg peaks of varying energies have to be shifter in the depth direction to conform a flat dose distribution distally (modulation width). The treatment nozzle ensures proper shaping of the proton beam in lateral as well as distal direction for a 3D dose distribution. There are two ways to laterally spread the beam: 1) Passive Scattering 2) Beam Scanning.

**Passive Scattering:**

Passive scattering involves introduction of materials of a high atomic number that scatter the proton beam striking it. This material is known as the scatterer and it spreads the pencil beam to have a Gaussian distribution profile. An aperture is placed ahead of the scatterer to block out unnecessary scatters beyond the central region. The scatterer, along with the aperture makes it appear as if the field is emanating from a virtual source. The size of this source depends on the amount of scattering material. The source size, therefore, is an intrinsic property. Although, the effect of source size can be mitigated till an extent by 'placing' the virtual source as far away as possible from the patient and by keeping the aperture close to the patient. This reduces the effects of source size on dose distribution.

The contribution of source size at the point of calculation (P) can be obtained by using the expression given below

$$\sigma_s(z_P) = \left(\frac{z_A - z_P}{SAD - z_A}\right)\sigma_s$$

Equation 6

where z denotes the z axis.
$z_P$ = z coordinate of point of calculation (P),
$z_A$ = z coordinate of aperture
$\sigma_s$ = projected penumbra width
SAD = isocenter to source distance (isocenter is the point of convergence of 3 axis of rotation in radiation therapy)

To account for heterogeneities in the path of proton beams, a range compensator is used. The range compensator introduces additional thickness in portions of irradiated area with lesser heterogeneities in depth direction to compensate for regions with higher densities

and hence, deposit uniform distal dose. Protons passing through thickness of range compensator experience additional scattering which contributes to another spread factor $\sigma_R$ expressed as

$$\sigma_R = L_P \theta_R$$

Equation 7

The total beam spread for dose delivery via passive scattering becomes:

$$\sigma_T^2 = \sigma_{MCS}^2 + \sigma_S^2 + \sigma_R^2$$

Equation 8

Dose deposition at point becomes:

$$D(P) = \sum \frac{1}{2\pi\sigma_T^2} \exp\left(\frac{-r_P^2}{2\pi\sigma_T^2}\right) D_\infty^R(dP) \left(\frac{SAD - z_P}{SAD}\right)^2$$

Equation 9

**Beam Scanning:**

This method uses dipole magnets that are orthogonal to each other. Proton beams are scanned laterally over field area. There is no requirement of a scatterer or an aperture due to which the inverse square correction factor is absent which is a contributing factor to total spread in case of passive scattering beam delivery. Scanning pencil beam method allows variation of energy. Varying energy and intensity allow for modulation of dose in the target volume. Although, a point to be noted is that as energy is varied, that changes introduced take time to act resulting in discrete layers of energy which is a limitation of beam scanning mode. The pencil beam is assumed to have non-diverging property. The beam is represented as a cone with an elliptical lateral distribution. By including the contribution to spread due to range compensator, the dose deposition at point P can be calculated as:

$$D(P) = \sum \frac{1}{2\pi\sigma_T^2} \exp\left(\frac{-r_P^2}{2\pi\sigma_T^2}\right) D_\infty^R(dP)$$

Equation 10

The pencil-beam algorithm is aided with more powerful computational hardware and software tools such as graphics processing unit (GPU), which by its parallelization capabilities, speeds up the algorithm to quite a good extent. However, this method has questionable accuracy in cases with complicated geometry and in-beam density variations, e.g., at bone-soft tissue interfaces. Another limiting factor of its application is the difficulty in determining the empirical data regarding the depth dose distribution of the pencil-beam. Though there is Bortfeld theory that incorporates effects of both range

straggling and initial energy distribution, and serves as a highly-accurate analytical model for dose evaluation in case of normal and oblique incidence of protons into a homogeneous target. It has been extended to a uniform broad beam with an initial Gaussian angular distribution as well. However, accurate analytical modelling of the depth-dose distribution in the target with localized tissue heterogeneities is still a major problem. When proton beams encounter heterogeneities in their path, the proton range is affected and results in degradation of the Bragg peak. This degradation is referred to as range dilution which in turn affects the overall dose distribution. We require algorithms to calculate range dilution in presence of heterogeneities.

## MONTE CARLO SIMULATION [5],[6]

Monte Carlo is a mathematical technique in which we perform repeated random sampling on an uncertain process or event, to obtain the average behaviour of the outcome. It is a statistical method and for accurate estimation of the outcome, a large number of sampling events are required and therefore a computer algorithm is used to model the chance process with random numbers and known probability distributions. In radiotherapy, Monte Carlo (MC) simulation is regarded as the most accurate method for prediction of delivered dose distribution. MC algorithm efficiently transports a particle through the defined medium by using particle physics for encoding and simulating the particle-particle interaction characteristics, with the help of theoretical models, parametrizations and experimental cross-sectional data.

### Proton transport:

The protons undergo an extremely large number of interactions per unit length traversing through the medium, which makes the transport kinematics complex. It is computationally not feasible to simulate all the individual interactions, and so the proton path is divided into a large number of small discrete steps. It is important to choose a proper step size in order to account for all the local heterogeneities and their effects on the dose distribution. Thus, the simulation is carried out one particle at a time, one step at a time, randomly sampling from the probability density functions representing the probability of particle interactions and their outcome, as given by the laws of physics.

The energy loss is calculated for each step using the stopping power values until the energy transfer to the electron reaches a threshold value, above which δ-electrons (high energy electrons generated from an ionization event that can cause further ionizations) are produced explicitly. The angle of deflection by scattering is determined for each step by sampling the angular distribution patterns predicted by the MCS theories. Thus, the simulation of continuous processes of proton energy loss and scattering continues until a discrete process of nuclear interaction or high energy δ-electron productions occurs. The switch from continuous to discrete processes might be a user variable in some MC codes. Successful secondary particles tracking during the simulation run allows us to account for the hard scatters and the probability of these interactions is calculated by using the measured cross-sectional data and nuclear models.

In MC dose calculation we need to decide which interactions to include. Although we need to generate all secondary particles in order to ensure energy conservation, it is not always necessary to track all of them. If the range of the generated particle is less than the size of a voxel in the patient, then its energy can be deposited locally. For a SOBP, nuclear interactions must be accounted for as they still play a role in the peak since the regions proximal to the Bragg peak contribute. It becomes even more important when using pencil beam scanning delivery method. Each pencil beam is surrounded by a nuclear halo, and even though the dose distribution is small for a single beam but it can be significant when adding multiple beams. For the purpose of dose calculation on a CT grid, the tracking of only primary and secondary protons is sufficient as they amount for approximately 98% of the dose, depending on the beam energy.

**Simulation: Modelling, User Input, and Output**

Data is fetched from the clinical treatment plan. The patient's CT scans are obtained and a patient-specific CT calibration, as described in detail below, is carried out for better dose-calculation accuracy. The beam characteristics at the entrance and the beam geometry are to be defined using the measured, manufacturer provided and treatment plan data.

The phase space distribution is a file that stores the result of particle tracking through the treatment head. Each particle is represented by a point in the phase-space with axes defining characteristics like energy, particle type and its direction cosines. These files may also store the particle histories, for example whether it is primary or secondary and other relevant parameters. For dose calculations the phase space is normally defined at a plane perpendicular to the beam axis between the treatment head and the patient. Different MC simulations are needed to be prepared for beams delivered using passive scattering and pencil-beam scanning.

For passively scattered beams, the treatment head needs to be meticulously modelled because the phase space of particles entering the patient depends on the configuration of the treatment head in a complicated manner. Thus, preparing beam models which are mathematical parametrization of the radiation field exiting the treatment head, is not feasible. Also, since each radiation field has unique treatment head settings and beam energy, the phase space data cannot be reused.

The configuration of the treatment head is determined from the range, modulation and the field size as prescribed in the treatment planning. For a double scattering system, its most important components are range modulator, first and second scatterer, snout, and the patient-specific aperture and range compensator. The time dependencies of the range modulator wheel are taken into account in the model. Beam current modulation is defined i.e., the modulation of the beam intensity in synchronization with the rotation of the modulator wheel. The machine-specific components of the treatment head are usually modelled using manufacturer blueprints and the geometries of patient field-specific apertures and compensators are usually provided by the planning system. A Computer-aided design (CAD) interface can also be used for the purpose of comprehensive modelling. The MC codes generally allows for the modelling of the components to be

done using 3-D geometric objects or their combinations. The materials, the treatment head is made up of, are specified using their recommended mean excitation energy values.

The number of protons to simulate on the $i_{th}$ step is given by:

$$N_i = N_T \frac{w_i}{sum(w_i)}$$

Equation 11

where $N_T$ is the total number of protons simulated and $w_i$ is the beam current weight. Beam weight is defined as the dose that would be delivered by the beam at the depth of maximum dose in a water-equivalent phantom, with the SOBP located at the isocenter.

The absolute dose that will be deposited at the target site can be predicted on the basis of ionization chamber readings obtained via simulation. But another and more efficient method of finding absolute dose is by relating the number of protons at the entrance of the treatment head to the beam weight, for a specified field. The beam weight can be determined by carrying out the simulation of beam delivery to the water-equivalent phantom placed according to the beam weight definition. The absolute dose $D_{abs}$ is then given by:

$$D_{abs} = W \frac{D_{sim}}{D_{ref}} \frac{P_{ref}}{P_{sim}}$$

Equation 12

where $D_{sim}$ is the simulated dose, $P_{sim}$ is the number of protons simulated, W is the beam weight, and $D_{ref}$ and $P_{ref}$ are the dose and the number of protons simulated for finding beam weight respectively.

There are certain uncertainties introduced by the application of Bethe-Bloch equation, like in the mean excitation energy values and therefore the simulated range doesn't match the range predicted by the treatment plan. So, we find the proton entrance energy as such the simulated range matches the requested range perfectly.

But in case of pencil beam scanning, beam parametrization can be performed and realistic beam models are feasible because the radiation field can be effectively defined by the fluence characteristics (*x*, *y*, beam energy, weight, divergence, and angular spread) of the pencil beams.

The pencil beams hardly interact with matter before reaching the patient and therefore we do not need to model the treatment head as extensively. The essential parts are the scanning magnets and any optional hardware used, for example an aperture to reduce the beam penumbra and optimise beam sharpness, in order to account for their scattering

effects. The code must be able to stimulate magnetic beam steering by modelling the magnetic fields affecting the particle tracking in the defined region.

The field characteristics obtained from the treatment planning system, is typically a list of beam spot positions on a plane upstream the patient parametrized by the x and y coordinates and the spot energy. This information is to be translated into magnetic field strengths (in units of Tesla), to be used as magnetic field settings in the MC simulation code. The fluence characteristics at the treatment head exit as obtained by the Monte Carlo simulation must match as those derived from experiments such as depth–dose distribution measured in water. This is achieved by determining and adjusting parameters in the MC code that results in best agreement with the experimental values. The energy of the beams is chosen such that the simulation gives the precise range in water. Thus, from the initial position of the beam spots, the treatment head and the scanning magnets, we can get the position and momentum at the end of the treatment head.

In a passive scattering system, most of the calculation time is spent on tracking particles through the treatment head which results in high computational time. But since pencil beam scanning method allows for the development and use of beam models, this enables the use of fast MC simulation in routine clinical practice.

The results of MC simulations are generally analyzed in form of histograms. The histograms are filled during the simulation run if certain conditions for a histogram bin are fulfilled, like for example a particle has deposited a said amount energy in a specific geometric region. Since a MC simulation provides the information about particle tracking either at the beginning or at the end of an individual step, so care needs to be taken while dealing with dose scoring in a MC system, especially at geometric boundaries to ensure that energy is deposited in target volume.

**Patient dose calculation:**

Now once we have the phase space distribution upstream of the patient, we can perform the dose calculation process.

Patient-specific CT calibration: The patient is modelled using a 3-D grid. The voxels are filled by CT numbers on the basis of the CT scan. The CT numbers in the voxels corresponding to any hardware that is present during the CT scan but would not be present during the actual treatment are replaced by the CT number of air. A patient-specific linear recalibration of the CT numbers is carried out. The CT number of air, which is generally defined as -1000 HU, is recalibrated to be equal to the average value of several sample CT numbers chosen randomly outside the patient. The recalibrated CT number of water, which is in general defined to be 0 HU, is obtained by subtracting a predefined CT number difference from the CT number of patient's tissue, like eye or cerebrospinal fluid, that have just slightly higher X-ray attenuation than water. The recalibrated CT numbers, $CT_c$ are given by:

$$CT_c = (CT_o + 1000)\frac{H_{water} - H_{air}}{1000} + H_{air}$$

Equation 13

where $CT_o$ are the CT numbers from the scan, $H_{air}$ and $H_{water}$ are the recalibrated CT numbers of air and water respectively.

For the patient dose calculation, the finite ranges of the proton beam need to be accurately determined which in turn requires the determination of proton stopping powers for the patient's anatomy. For each voxel on the recalibrated grid, the CT number is converted to density and material composition, using available models like W. Schneider method. The MC code then determines stopping power and many other useful parameters form these material properties. It must be ensured that the stopping powers calculated by the MC simulation matches with those used for dose calculation in the clinical planning, in order to facilitate a fair comparison. This can be done using appropriate correction factor.

Dose-to-water conversion: In radiotherapy, dose is traditionally expressed in terms of dose-to-water. But unlike analytical dose calculation algorithms that uses water-equivalent physics models and stopping powers relative to water, MC simulation works with material properties converted from CT numbers and therefore it provides us with dose calculated in terms of dose-to-tissue. This is a major advantage of using MC simulation for dose calculation. But since our present clinical experience and quality assurance is based on dose-to-water, and also to allow for a proper comparison between dose distribution results derived by using pencil beam algorithms and MC simulations, we must convert the dose-to-tissue $D_m$ as generated by MC code to its water-equivalent dose $D_w$.

This can be done using the simple formula:

$$D_w = D_m \frac{S_w}{S_m}$$

Equation 54

where $S_m$ is the mass stopping power of the medium and $S_w$ is the mass stopping power of the particle in water. This conversion using energy independent relative stopping powers is sufficiently accurate (within ~1%) in most cases.

MC dose calculation is a statistical method and therefore its precision depends highly on the total number of particles simulated. For attaining the accuracy required for clinical purpose, an enormously large number of particles are required which leads to high computational costs and therefore longer execution times. Therefore, this method is still applied mainly to re-calculating existing treatment plans in clinical settings, for verifying the accuracy of analytical methods of dose calculation in research studies and for secondary dosimetric calculations.

Some general-purpose MC codes used for particle transport are Geant4, FLUKA and MCNPX but they are too slow for simulations in a phantom with inhomogeneities. Over

years now, numerous efforts have been put into accelerating the MC dose calculation process and increasing its efficiency. Simplified algorithms are developed in an effort to ease the computational burden. Advanced computational hardware and software, for example Graphics processing units (GPUs), are put into use to provide for the required large-scale computational power. With reduced computational time, it becomes affordable to consider more complex physics in the modelling process, resulting in considerably enhanced dose-calculation accuracy. This proves out to be especially resourceful in cases with complicated geometry and large heterogeneities and is a step closer in dealing with the human anatomy with all its complexities, for dosimetric purposes.[5]

## RANGE UNCERTAINTY AND THE ROLE OF DOSE CALCULATION METHODS [7],[11]

Considerable amount of uncertainty is introduced in the range of proton beams during imaging, patient setup, beam delivery and dose calculation. This uncertainty in the range is a major challenge in the use of proton therapy in the commercial picture, as with the advent of precise positioning of the dose arises the increased ramifications of range uncertainties. In order to make our treatment plan effective in the face of all range uncertainties, we add a range margin to the prescribed range such that if the dose is deposited within this optimized range, then our target volume receives the required radiation. This process becomes even more complex in case of IMPT, as the beams may also stop within the target volume.

Uncertainties independent of the dose calculation are mainly those in commissioning, compensator design, beam reproducibility and patient setup. The uncertainty introduced during dose calculation can be from the process of determining proton beam range from the patients' CT scan and from the dose calculation algorithms itself. Furthermore, there are uncertainties due to radiobiological considerations such as the uncertainty due to variations in relative biological effectiveness (RBE) at the distal fall-off. Here in this paper, we only discuss the uncertainties that are introduced by dose calculation and some mitigation strategies with improvement in the calculation techniques, especially with the increased use of Monte Carlo in clinical treatment planning.

As discussed earlier, in order to determine the proton range, a conversion is to be made between the CT numbers and proton stopping powers. This requires certain assumptions to be made on the composition and ionization potential of the tissues. There can also be degeneracy and the same CT X-ray attenuation might correspond to different stopping powers. The uncertainty due to CT conversion is smaller when using MC simulations than from when using analytical methods. This is because the MC method assigns density and material composition to CT numbers which are then used to calculate the stopping powers rather than using the relative stopping powers as is customarily done in the case of pencil-beam algorithm. The uncertainties due to noise in CT images, calibration and CT resolution have a very limited impact on the stopping powers. These uncertainties arising from CT imaging and conversion are generally systematic for most of the tissue traversed in the beam path and therefore their total magnitude is proportional to the range of the beam. These uncertainties can be heightened in the presence of CT artifacts like the

presence of metallic materials in or on the patient, which degrade the quality of CT images and thus affecting the range. For a detailed discussion on uncertainties caused by CT conversion and resolution, primarily with the use MC simulation refer *Paganetti, 2012.*

**Range uncertainties due to dose calculation algorithms:**

A variety of pencil-beam models have been proposed over the years, incorporating theories like Fermi-Eyges for transportation of pencil beams through a stack of different materials. Even though the Fermi-Eyges theory takes into account both stopping and MCS, and therefore helps in dealing with the longitudinal as well as transverse heterogeneities of such mediums. But a stack of homogenous slabs is still no way near characterizing the complex, heterogeneous regions of patient's anatomy. And thus, analytical methods like the pencil beam algorithms are not very accurate in calculating the proton range while dealing with complex geometries and density variations. The regular and structured heterogeneities introduced in the patient modelling generally affects only a small region of the distal dose distribution and leads to a simple widening of the distal fall-off but the effects of complex human anatomy on the dose distribution are hard to predict.

Most pencil beam algorithms project range on the basis of water-equivalent depth in the patient for individual beam spots and does not take into account the position of inhomogeneities relative to the Bragg-peak depth. The range degradation due to MCS in complex structures cannot be predicted by simply using stopping powers of the materials in the beam path and their water-equivalent lengths, as such modelling only predicts a shift in the distal fall-off. There is also a major dose discrepancy in the entrance region as most analytical algorithms do not account for aperture scattering. While these effects are local for large fields but they might have serious consequences in case of small fields like those used in the head and neck region, and might affect majority of the target volume.

Even though by using MC, the range uncertainty caused by MCS in complex patient anatomy is mitigated to a large extent but there are uncertainties that are introduced while using MC methods too. The user-defined parameters and the tracking parameters like the step-size have a significant impact on the accuracy of the MC results. There can be uncertainties in the implementation of physics in encoding the particle interactions using theoretical models and experimental data, with the help of parametrizations and data interpolation. For example, even though the physics of MCS is very well understood and explained by the Moliére's theory, but the accuracy of our simulation result depends on the probability distribution we are using for sampling the transverse distribution.

Though there are considerable uncertainties in nuclear interaction probabilities but fortunately they are inconsequential for range prediction in dose calculation. But the secondary neutrons reaching the patient are a concern while assessing the potential side effects and in shielding design studies. The analytical dose calculation methods cannot calculate the neutron generated dose because they are not commissioned for low doses, as the low neutron doses are inconsequential in treatment planning. MC method proves out

to be useful in simulating the secondary neutron doses and to study the effect of treatment head design on neutron production.

Also, it must be noted that most of the MC codes used today were originally generated for high energy physics applications and might not be very well attuned to the purpose of dose calculation in proton therapy and therefore require proper adjustments. The accuracy of the physics settings might depend on the particle being dealt with and on the energy range of interest.

While using MC for a passively scattered system, as explained in detail earlier in the paper, we need to model the entire treatment head and simulate beam transport through it to obtain the phase space upstream of the patient. Apart from the uncertainty in the I-values, there can be other uncertainties too. The manufacturer blueprint of the treatment head components and the built device can have slight variations that are left unaccounted for. Moreover, there can be discrepancy in the material compositions of the treatment head provided to be used for modelling. Certain of these uncertainties cannot be overcome as it cannot be always made possible to obtain the faultless data on geometry and material composition of the treatment head but what can be done to reduce the impact of this modelling uncertainty is an optimization of the time-dependent beam current modulation process.

For dose calculation of a pencil-beam scanning system, small uncertainties in the nuclear halo or MCS might be insignificant for a single beam but they can lead to large uncertainties when multiple beams are added. An investigation into the source of particles contributing to the low-dose envelope around the beam's central axis in done using the MC technique in *Sawakuchi GO, Titt U, Mirkovic D, et al. 2010.*

One of the major lacking of pencil beam algorithms is their questionable accuracy in the presence of lateral heterogeneities. A *heterogeneity index* parametrizes the lateral tissue heterogeneities for a beam spot and thus is useful in determining whether significant differences would be present in the predicted dose distributions resulting from pencil beam algorithm and MC algorithm. The heterogeneity index can thus be used in identifying those cases where MC dose calculation is desired and would serve best results.

## DISCUSSION

The improved depth-dose characteristics and the rapid dose fall-off of proton therapy allows for a considerable reduction in the integral dose delivered to the patient by achieving a highly localised dose deposition while sparing the normal tissues from unnecessary irradiation. Hence, dose escalation can be easily performed while mitigating radiation toxicity in surrounding normal tissues. Moreover, proton radiation has higher ionisation density than photon radiation which results in an increased cell-killing efficiency. Despite these seemingly revolutionary advantages of proton therapy over the traditional methods, its use is still very limited as per end of 2021, close to only 280,000 patients have been treated worldwide with proton therapy.[8]

The efficiency achieved in proton dose calculations so far is still unsatisfactory and limits the potential of proton therapy. Presently, pencil beam algorithms are employed in most clinical settings due to their short calculation times, which is especially useful for IMPT. But pencil beam algorithms have accuracy limitations and are less reliable in the presence of heterogenous tissue. Though MC simulation provides for the accuracy required in clinical settings and it is likely that MC is the future of dose-calculation, the computational efficiency of current MC codes is not optimised for routine clinical use. Certain research areas could be intensively explored to further accelerate the proton dose calculations. It is always possible to increase the efficiency of the dose calculation algorithms with advancement in the hardware technology such as with the development and use of faster GPUs. Another field of research of importance is the development of new simpler yet efficient algorithms to cut down the computational cost. Algorithm-based acceleration is usually more efficient than hardware-based acceleration when it comes to boosting the processing speed.[9]

Dose calculation uncertainties are generally taken into account during treatment planning by avoiding pointing the beam towards a critical structure and by adding safety margins. As a result of these precautions, no major difference of clinical significance is observed in the dose calculation results from pencil beam and MC algorithms. Though adding range margins in order to deal with the uncertainties makes the treatment plan robust against range uncertainty, but it does come at a cost. Additional dose is delivered because of the range margins and many other compromises are to be made between target coverage and dose to the organ at risk when designing treatment plans, making the treatment delivered to the patient suboptimal.

At the Massachusetts General Hospital (MGH), an uncertainty margin of 3.5% of the range in water (based on the uncertainty associated to CT imaging and conversion) plus an additional 1mm (to account for random errors in beam delivery and patient set-up) is used. Other proton facilities also quantify range using similar margin recipe guidelines. The range margin quantification depends highly on the location of the target lesion. Additional margins are added for example in cases where issues regarding patient immobilization or organ motion are faced during the procedure. Also, if the initial treatment plan does not accurately reflect the patient anatomy during the actual procedure, for example in the case of change in patient's weight. This 3.5% + 1mm margin was derived on the basis of CT technology and resolution of the early 1980's and it does not include any uncertainties introduced by the dose calculation methods, except those associated with the water equivalent density.[11]

In a relatively homogeneous tissue, the additional uncertainty due to dose calculation is negligible. The improved accuracy of MC method over pencil beam algorithm has no influence on the conservative treatment margins as the main source of uncertainty i.e., the uncertainty in the mean excitation energies remains. Therefore, in the presence of homogenous tissue in the beam path, calculation results obtained from analytical dose calculation are precise enough and the use of this method fulfils both needs of speed and sufficient accuracy required for an efficient treatment planning. But in the presence of critical heterogeneities and complex geometries, pencil-beam dose calculation algorithms can introduce an uncertainty up to about ±2.5% and MC algorithms proves out to be the

better alternative. This is because MC simulation method can almost completely eliminate the uncertainties due to approximate calculations of proton scattering that are used in analytical methods as they work by simulating the individual proton-matter interactions. More extensive studies are needed to understand the impact of dose-calculation uncertainties in order to reduce the mitigable ones. Studies aimed at identification of clinically significant differences between pencil beam and MC based dose calculations may also help in improvement of the current pencil-beam methods and in recognizing the potential checkpoints where MC simulation could be utilized during the treatment plan optimization.

Organ motion, for example in treatment of tumours in the lung due to the motion associated with the breathing cycle, is a major challenge to the use of proton therapy till date. Currently, we deal with this uncertainty by adding additional margins to the clinical target volume. But this takes away the principal advantage of using proton therapy that is the high precision of dose placement. Thus, the need is to take the motion effects into account during the treatment planning itself. When using pencil beam algorithms, it turns out to be a very difficult task. Since we have to perform ray-tracing for time dependent density distributions which increases the calculation time, rendering it impractical for clinical use. But it can be realised using MC and that too without any significant increase in the computation time than the static MC. First, we have to obtain density distribution function of the target with time, for example using a set of time dependent CT grids. Then before simulating the particle history, the density in each voxel is to be chosen randomly from this density distribution function. As such, the motion effects can be modelled and accommodated using MC algorithms quite efficiently making it the preferable alternative for use in treatment planning in near future for moving treatment sites.

Reduction in range uncertainties has been a major field of research in advancing proton therapy. In vivo beam monitoring methods like Positron emission tomography (PET) and the more recent Prompt γ-ray detection are being studied and used for range verification on basis of which the treatment plan could be adjusted to ensure target volume coverage while maintaining reduced margins. MC simulation can be used to generate theoretical PET images using the prescribed radiation field which can be compared with the measured PET distributions for treatment verification purpose. This is one of the many other applications of MC simulation. Though analytical methods could also be used but the approximations employed in these methods might lead to the treatment being adjusted on basis of a dose distribution that slightly deviates from the actual dose distribution in the patient. A detailed discussion on modelling of prompt γ-ray emissions using MC codes and additionally also on improved MC dose calculation accuracy if the proton beams pass though implants or inhomogeneous tissue can be found in *Joost M. Verburg, 2015*. Direct dose measurement can be performed for specific treatment sites by placing dosimeters inside the human body and magnetic resonance imaging (MRI) can be used to evaluate range information due to tissue changes on longer time scales. Moreover, CT technology has considerably improved since the early 1980's. Incorporating the highlights of the above discussion, and a more elaborate study on the potential refinement of the range margins with the increasing use of MC, a new estimate of the range

uncertainties is required. Such a study and estimation of range uncertainties for the static case is carried out in *Paganetti, 2012.*

There are also certain other factors that govern the use of proton therapy in clinical settings. Whether the procedure is cost effective, what kind of patients would benefit the most, how well does it work alongside other treatment modalities such as surgery and chemotherapy, to what extent does proton therapy reduce treatment toxicity and can it finally improve the life quality of the patients. Until these questions remain unanswered due to the lack of availability of quantitative information, it is challenging to generate concluding remarks that demonstrate the true value of proton therapy. Nevertheless, the future of proton beam therapy is very promising.

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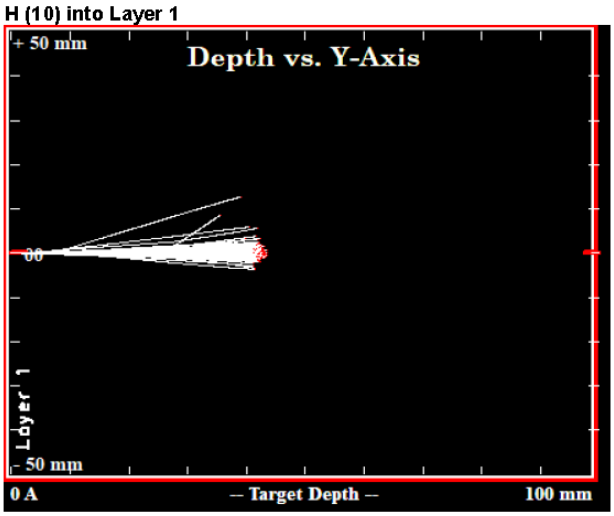



*1044 Ions Calculated*
Ion Type = H
Ion Energy = 50 MeV
Ion Angle = 0

Calculation Parameters:

| | |
|---|---|
| Backscattered Ions | 0 |
| Transmitted Ions | 0 |
| Vacancies/Ion | 178.0 |

| ION STATS | Range | Straggle |
|---|---|---|
| Longitudinal | 41.9 mm | 540. um |
| Lateral Proj. | 586. um | 913. um |
| Radial | 916. um | 813. um |

Type of Damage Calculation
Quick: Kinchin-Pease

Stopping Power Version
SRIM-2008

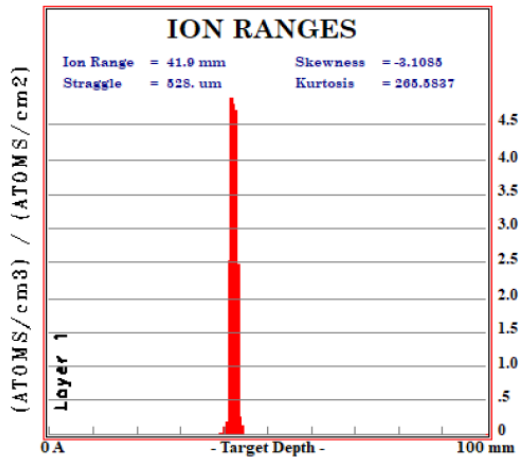
| % ENERGY LOSS | Ions | Recoils |
|---|---|---|
| Ionization | 99.95 | 0.02 |
| Vacancies | 0.00 | 0.00 |
| Phonons | 0.01 | 0.02 |

Target layers:

| | Layer Name | Width (A) | Density | H (1.008) | O (15.999) | H (1.008) | Solid/Gas | Stop Corr. |
|---|---|---|---|---|---|---|---|---|
| 1 | Layer 1 | 1000000000 | 0.523 | 0.33333 | 0.33333 | 0.33333 | Solid | 1 |
| | Lattice Binding Energy | | | 3 | 3 | 3 | | |
| | Surface Binding Energy | | | 2 | 2 | 2 | | |
| | Displacement Energy | | | 10 | 28 | 10 | | |

[Figure 1]

H (10) into Layer 1




***2350 Ions Calculated***
Ion Type = H
Ion Energy = 50 MeV
Ion Angle = 0

Calculation Parameters:

| | |
|---|---|
| Backscattered Ions | 0 |
| Transmitted Ions | 0 |
| Vacancies/Ion | 179.5 |

| ION STATS | Range | Straggle |
|---|---|---|
| Longitudinal | 41.9 mm | 528. um |
| Lateral Proj. | 579. um | 848. um |
| Radial | 922. um | 740. um |

Type of Damage Calculation
Quick: Kinchin-Pease

Stopping Power Version
SRIM-2006

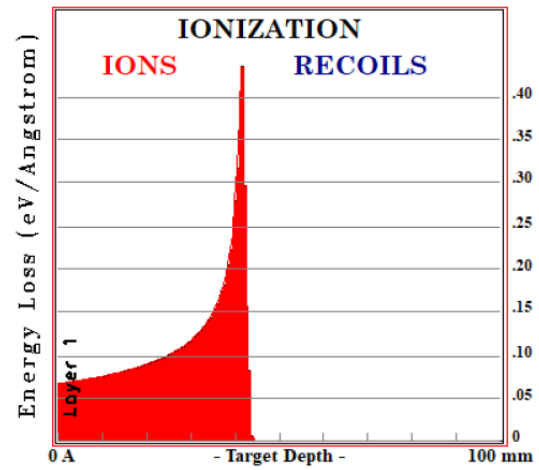
| % ENERGY LOSS | Ions | Recoils |
|---|---|---|
| Ionization | 99.96 | 0.02 |
| Vacancies | 0.00 | 0.00 |
| Phonons | 0.01 | 0.02 |

Target layers:

| | Layer Name | Width (A) | Density | H (1.008) | O (15.999) | H (1.008) | Solid/Gas | Stop Corr. |
|---|---|---|---|---|---|---|---|---|
| 1 | Layer 1 | 1000000000 | 0.523 | 0.33333 | 0.33333 | 0.33333 | Solid | |
| | Lattice Binding Energy | | | 3 | 3 | 3 | | |
| | Surface Binding Energy | | | 2 | 2 | 2 | | |
| | Displacement Energy | | | 10 | 28 | 10 | | |

[Figure 2]

H (10) into Layer 1




***2660 Ions Calculated***
Ion Type = H
Ion Energy = 50 MeV
Ion Angle = 0

Calculation Parameters:

| | |
|---|---|
| Backscattered Ions | 0 |
| Transmitted Ions | 0 |
| Vacancies/Ion | 180.5 |

| ION STATS | Range | Straggle |
|---|---|---|
| Longitudinal | 41.9 mm | 525. um |
| Lateral Proj. | 578. um | 840. um |
| Radial | 922. um | 734. um |

Type of Damage Calculation
Quick: Kinchin-Pease

Stopping Power Version
SRIM-2006

| % ENERGY LOSS | Ions | Recoils |
|---|---|---|
| Ionization | 99.96 | 0.02 |
| Vacancies | 0.00 | 0.00 |
| Phonons | 0.01 | 0.02 |

Target layers:

| | Layer Name | Width (A) | Density | H (1.008) | O (15.999) | H (1.008) | Solid/Gas | Stop Corr. |
|---|---|---|---|---|---|---|---|---|
| 1 | Layer 1 | 1000000000 | 0.523 | 0.33333 | 0.33333 | 0.33333 | Solid | |
| | Lattice Binding Energy | | | 3 | 3 | 3 | | |
| | Surface Binding Energy | | | 2 | 2 | 2 | | |
| | Displacement Energy | | | 10 | 28 | 10 | | |

[Figure 3]