Proton Beam Therapy-based Computation in the Treatment of Human Ovarian and Liver Cancer Using SRIM

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Abstract
Proton beam therapy is a promising technique used to cure various types of cancer diseases in the human body. This technique can selectively damage cancer cells while leaving surrounding cells unaffected thereby minimizing collateral damage to the healthy cells. The position and the width of the cancerous cells are determined to calculate the energy required to destroy the affected cells. The energy loss to the damaged cells and other body parts is calculated separately with high accuracy. Computational analysis indicates that proton beams with energies of 46 MeV, 47 MeV, and 48 MeV effectively destroy localized cancerous cells of the ovary from the epithelial cells to the more invasive cancerous growth while proton beam energy range of 50 MeV to 89 MeV should be considered for the treatment of liver cancer of both the periphery tumours and tumours in the hilum. Transport of ions in matter (TRIM) data shows that more than 80% of proton energy is given off during ion bombardment at Bragg’s peak, while the remaining percentage is lost by phonon production and by recoils.

Keywords: Proton Beam Therapy, SRIM, human ovary, human liver, carcinoma

Introduction
Proton beam therapy (PBT) is a particle therapy technique that employs a proton beam to irradiate affected tissues in the human body. Owing to its excellent physical properties and dosimetry parameters, PBT has been used in a variety of cancer treatments for example Wilson proposed PBT for the first time in 1946 [1]. Researchers at the Lawrence-Berkeley National Laboratory published the first PBT case series after a 12-year wait. Several other proton treatment facilities emerged throughout the world during the next few decades, and PBT has now been utilized in the clinical environment for more than 60 years, treating tens of thousands of patients with various forms of cancer cases. The appropriate application of PBT has led to fewer adverse effects and higher therapeutic efficacy compared with conventional radiotherapy (RT) using X-ray beams. Thus, facilities for PBT are being built worldwide, despite the requirement for costly equipment [2–4]. Over the past decades, with increasing PBT applications worldwide, the number of new programs under development has been growing. The reason for this is that the proton dose distribution that may be achieved is generally superior to the dose distribution of conventional photon radiation therapy (PRT). PBT may improve the survival rate of patients by improving the local tumour treatment rate, while reducing injury to normal organs, resulting in fewer radiation-induced adverse effects. The clinical benefits of PBT have been established in terms of fewer side effects when compared to photon treatment. However, the use of PBT is controversial due to the high treatment costs associated with proton facility development and maintenance. When compared to photon treatment, however, the higher cost may be justified because of the improved quality of life and lower expenditures associated with post-exposure illness and care. More research and discussion are needed to address the use of PBT in various malignancies, as well as how to maintain patients’ quality of life while achieving a high cure rate [1, 5]. In recent decades, as the number of PBT applications around the world has grown, so has the number of new programs in development. Because the proton dosage distribution that may be achieved is generally superior to the photon dose distribution, this is the rationale. PBT can potentially improve patient survival rates by enhancing local tumour treatment rates while reducing damage to normal organs, resulting in fewer radiation-induced adverse effects. Compared to typical photon RT, heavier subatomic particles can convey their energy more accurately to the tumour, with less scattering to adjacent tissues. PBT is associated with obvious benefits, such as reducing the volume of irradiated normal tissue and improving the conformability and the quality of the target area. Data showed that 11.5% of proton patients experienced a grade three or higher side effect. In the photon group, 27.6% experienced a grade three or higher side effect. A weighted analysis of both patient groups, which controlled for other factors that may have led to differences between the patient groups, found that the relative risk of severe toxicity was two-thirds lower for proton patients compared to photon patients [6, 7].

[ARTICLE HISTORY]
Submitted
July 13, 2023
Revised
October 3, 2023
First Published Online
October 29, 2023

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doi.org/10.62050/ljsir2023.v1n1.166
Importantly, overall survival and disease-free survival were similar between the two groups, suggesting that the reduction in toxicity seen with proton therapy did not come at cost-effectiveness. Further studies and discussions are required to make proton therapy cost-effective to address its use in several types of cancer and to maintain the quality of life of patients while achieving a high cure rate.

Apart from the adverse effects of exposure to energetic particles due to carcinogenesis and degenerative disease, proton therapy in the treatment of cancer is a promising approach to curbing the growth of cancerous cells in the body [1, 7–11]. The damage (Bragg’s peak) due to ionization and recoils in the target atoms during proton bombardment at a certain energy can be localized to destroy cancerous cells [4, 11]. Bragg peak is a distinct property of protons and when it reaches cancer tissues after penetrating through the normal tissues in the body, it releases an immense amount of radiation energy to kill the cancer cells and subsequently, it disappears instantly.

This work reports the stopping range of ions in matter and the energy deposition by the target atoms in the human liver and ovary when the composition of a healthy human liver and ovary in a computational phantom are bombarded with protons at varying energies using SRIM-2013 (the Stopping and Range of Ions in Matter) [5, 12]. Following this section of the study is a detailed description of the materials and methods in the computation, the composition of the targets (human liver and the ovary), and the SRIM setup of the computation phantom. The remaining part of the article is discussed under results and discussion, and conclusion.

### Materials and Methods

#### Human liver

The liver is the largest solid organ in the human body located under the rib cage in different configurations according to body size (Fig. 1) and plays a significant role in the vital metabolic functioning of the body these functions include removing waste products and foreign substances from the bloodstream, regulating blood sugar levels, and creating essential nutrients. During development, liver size increases with increasing age, averaging a 5 cm span at 5 years, and attaining an adult size average of about 8.6 cm (male and female) from age 15, with an average volume of 1624 cm$^3$ [11] and weighing about 1.5 kg. However, the size depends on several factors including age, sex, body size, shape, and to what extent the liver is healthy[ 13, 14].

![Figure 1: Different configurations of the human liver frontal view (in shaded black) in the rib cage according to body size [14] considered in the computational phantom.](image)

This computation is useful for the treatment of carcinomas that originated and are localized in the liver such as hepatocellular carcinoma, intrahepatic cholangiocarcinoma and hepatoblastoma, not the ones that spread from other regions of the body. We adopted the stoichiometry composition of the human liver from the previous work [15, 16] described in Table 1.

### Table 1: Stoichiometric composition of human liver

<table>
<thead>
<tr>
<th>Elements</th>
<th>Atomic No.</th>
<th>Weight (AMU)</th>
<th>Atomic %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrogen</td>
<td>1</td>
<td>1.008</td>
<td>11</td>
</tr>
<tr>
<td>Carbon</td>
<td>6</td>
<td>12.01</td>
<td>4.1</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>7</td>
<td>14.00</td>
<td>1.2</td>
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<tr>
<td>Oxygen</td>
<td>8</td>
<td>15.99</td>
<td>82.5</td>
</tr>
</tbody>
</table>

### Table 2: Stoichiometric composition of the human skin

<table>
<thead>
<tr>
<th>Elements</th>
<th>Atomic No.</th>
<th>Weight (AMU)</th>
<th>Atom (%)</th>
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<tbody>
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<tr>
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<tr>
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<td>15.99</td>
<td>59.0</td>
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<tr>
<td>Sodium</td>
<td>11</td>
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<tr>
<td>Sulfur</td>
<td>16</td>
<td>32.06</td>
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<tr>
<td>Chlorine</td>
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</tr>
<tr>
<td>Potassium</td>
<td>19</td>
<td>39.09</td>
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Human skin
To achieve a more realistic approach in our simulation, we have included the first layer as human skin. This skin consists of both the epidermis and dermis. We have used an average thickness of 0.138 cm, which is based on the average thickness of human skin on the abdomen and chest [17, 18] with a density of 1.09 g/cm$^3$. The stoichiometry of the human skin is taken from the SRIM 2013 data archive (Table 2).

Stoichiometric composition of human skin
The stoichiometric composition of human skin refers to the ratio of different elements present in the human skin [15, 17, 19]. These elements play a vital role in the structure and function of the skin. It helps determine the chemical makeup of the skin. These include carbon, oxygen, hydrogen, nitrogen, sulfur, potassium, and trace amounts of other elements.

Human ovary
The female reproductive system consists of internal organs such as the uterus, cervix, vagina, ovaries and fallopian tubes. The external structures include the breasts and labia. The ovaries are two small almond-shaped organs that lie on either side of the uterus in a depression called the ovarian fossa. They are connected to the uterus by Fallopian tubes which are hollow muscular tubes. The ovaries’ (Fig. 2) primary function is to store the ova (eggs) that a female child is born with; these ova reach maturity at puberty and every month one ovum is released during menstruation. The ova passes through the fallopian tubes into the uterus. The ovaries also produce oestrogen and progesterone which are the female hormones. They regulate menstruation and the development of sex organs. The ovary is made up of three different cell types including epithelial cells, germ cells, and stromal cells. Tumours can develop in any of these cells, when these cells become abnormal, they can divide and form tumours. These cells can also invade or spread to other parts of the body.

![Figure 2: The female reproduction anatomy showing the ovary](image)

The stoichiometric composition of the human ovary
The stoichiometric composition of the human ovary in Table 3 refers to the ratio of different elements present in the ovary. The human ovary is composed of various types of cells, including oocytes (egg cells) and supporting cells. They contain elements like carbon, oxygen, hydrogen, nitrogen and other trace elements [15]. The ovary is 3 cm long, 2.5 cm wide and 1.5 cm thick having a density of 0.252 g/cm$^3$.

<table>
<thead>
<tr>
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</tr>
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<td>Nitrogen</td>
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</tr>
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The stoichiometric composition of muscles equivalent
In the computational phantom of the human ovary, we introduce the International Commission on Radiation Units and Measurement (ICRU) muscle equivalent in the SRIM data archive to account for the soft tissues surrounding the ovary. The muscles equivalent has a width of 9.8 mm and 1.99 g/cm$^3$ density. The stoichiometric composition referred to in Table 4 is the atomic makeup, which comprises elements such as hydrogen, carbon, nitrogen and oxygen [1].

<table>
<thead>
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<th>Atomic %</th>
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<td>74.2</td>
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Stopping power and range
The stopping power describes the energy loss per unit path length when charged particles, such as protons, propagate through matter [3, 4, 11, 20]. Charged particles lose their energy mainly through collisions with atomic electrons of the traversed medium. As a result of these collisions, the electrons can be raised to a higher shell (excitation) or ejected from the atom (ionization). The range of the proton is determined by the inelastic interactions with atomic electrons. The stopping power, \( S \), can be described by the Bethe-Bloch formula,

\[ S = -\frac{dE}{dx} = 2\pi N_p a^2 Z \frac{\gamma^2}{\rho} \ln \left( \frac{2m_e\gamma^2\rho}{m}\right) - 2\beta^2 - 2\gamma \frac{\rho}{m}\] (1)

\( r_e \) classical electron radius given as 2.818 fm, \( m_e \) mass electron, 0.511MeV/c, \( Z \) atomic number of absorbing material, \( c \) is the speed of light, \( v \) speed of the incident particle, \( z \) charge number of incident particle, \( I \) mean excitation potential, \( C \) shell correction, \( N_i \) Avogadro’s number. \( W_{\text{max}} \) Maximum energy transfer in a single collision, \( A \) atomic mass of absorbing material, \( \rho \) density, \( \beta = v/c \) of incident particle, \( \gamma \) Lorentz factor \( 1/2 \), \( \delta \) density correction.

Energy loss rate
The energy loss rate of ions, or linear stopping power, is defined as the quotient of the energy loss rate in a way that is independent of the mass density; the mass stopping power is defined as

\[ \frac{\Delta E}{\Delta x} = \frac{dE}{dx} \] (2)

where \( \rho \) is the mass density of the absorbing material. Stopping power is defined as a beam, not a particle. The energy loss rate may be described by several mathematical formulae. The simplest, yet still remarkably accurate, formula is based on the Bragg-Kleeman (BK) Rule which was originally derived for alpha particles and is given by

\[ \frac{\Delta E}{\Delta x} = \frac{dE}{dx} = \frac{\alpha \gamma^2}{\beta^2} \] (3)

where \( \rho \) is the mass density of the material, \( \alpha \) is a material-dependent constant, \( U \) is the initial energy of the proton beam, and the exponent \( p \) is a constant that considers the dependence of the proton’s energy or velocity. Values of \( \alpha \) and \( p \) may be obtained by fitting to either ranges or stopping power data from measurements or theory. By integrating the reciprocal of the stopping power in Equation 1 we obtained the average range \( R \) in Equation 4.

\[ R = \int_0^R \frac{dE}{\rho} \approx \int_{\beta}^{\beta+1} \frac{\Delta E}{\rho} \] (4)

The range is dependent on the proton energy and the characteristics of the biological matter.

SRIM set-up
Here we describe the physical model of the SRIM set-up for the TRIM (the Transport of Ions in Matter) calculations of our sample (Fig. 2). To achieve consistency in the calculation and low uncertainty, we used 10,000 incident ions. This is a good compromise between accuracy and computation time.

The energy transferred to the recoil and the ionization data files were used to calculate the energy deposited per target depth at the Bragg’s peak \( (T_{\text{dep}}) \) (Eqn. 5).

\[ T_{\text{dep/depth}} = \left( E_{\text{recoil}} - E_{\text{ioniz}} \right) \times 10000 \] (5)

The effective displacement energy \( (E_d^{\text{eff}}) \) of the targets is calculated using Equation 6.

\[ E_d^{\text{eff}} = \left[ \sum S_n \right]^{-1} \] (6)

where \( E_{d,n} \) and \( S_n \) are the displacement energy and the stoichiometry fraction of the nth ions, respectively (Tables 5 and 6) [2, 21].

The default SRIM surface binding energy (\( \leq 8 \) eV) (Table 6) was used during all calculations with lattice binding energy (3 eV). The computational set-up of the layers is shown in Figs. 3 and 4.
Table 5: Displacement energy ($E_{d,n}$) of the constituents’ atoms

<table>
<thead>
<tr>
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<th>H</th>
<th>C</th>
<th>N</th>
<th>O</th>
<th>S</th>
<th>Cl</th>
<th>Na</th>
<th>K</th>
<th>$E_{d,n}$ (eV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>eV</td>
<td>10</td>
<td>28</td>
<td>28</td>
<td>28</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>11.77</td>
<td></td>
</tr>
</tbody>
</table>

Table 6: Surface binding energy of the constituents’ atoms

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<th>O</th>
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<td>2.88</td>
<td>2.00</td>
<td>1.12</td>
<td>0.93</td>
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</table>

Results and Discussion

SRIM’s quick calculation of damage, or Q-C, only tracks the targeting ion up to the initial impact of the projectile on the target. While this can provide insight into the primary effect of protons on the target ions, it doesn’t account for the secondary ions due to recoils and collisions that occur when the projectile interacts with the atomic species in the target. To account for the secondary and tertiary ions due to recoils we run the SRIM code in the full cascade (F-C) mode.

**Proton beam on liver computation**

When a proton is directed towards a target, it releases its energy at a specific depth, known as the Bragg’s peak. This is the targeted area of the tumour. More than 80% of the proton’s energy is deposited at this point, while the remaining percentage goes to the recoil ions. However, at 20 MeV, the energy deposited at the Bragg’s peak is less than 50%, and it does not penetrate beyond the skin layer. Thus, depending on the location and depth of the affected area, proton beam therapy with energies ranging from 50 MeV to 89 MeV is enough to treat liver carcinoma cells of both the peripheral and hilum tumours.

![Figure 5: Proton beam energy deposition ($T_{dep}$) per Target depth of the human liver at different energies showing the Bragg peaks](image-url)

Proton of 50 MeV as a stopping range of less than 3 cm (Table 7) into the target layers could be used for the treatment of the epithelial scarring of the liver in the periphery tumour with little to non-damage to the surrounding organs and tissues; while proton at higher energies (60 MeV to 89 MeV) could be effective against deep-rooted liver carcinoma (Table 7). The property and the characteristic Bragg’s peak as shown in Fig. 5 makes PBT a very promising method in the treatment of cancer cells in the body that will preserve the surrounding healthy cells.

![Figure 6: Proton beam energy deposition ($T_{dep}$) per Target depth of the human ovary at different energies showing the Bragg peaks at 46 MeV, 47 MeV, and 48 MeV](image-url)

The ranges in Table 8 are where the Bragg peak occurs whereby the proton deposited the highest energy that can destroy the localised cancer cells in the ovary for example in Fig. 6 this occurs at the second peak consistent with the location of the ovary.
**Conclusion**

According to our calculations, SRIM is suitable for estimating the amount of proton energy needed, proton stopping range, and deposition energy required for proton beam therapy (PBT) in the treatment of liver and ovarian cancer [1]. PBT is particularly useful in treating localized tumours. In the liver computation phantom, over 80% of the projectile energy is deposited at Bragg’s peak, whereas the ovary computation shows a double peak with only 20% or less of the energy deposited in the soft tissues and muscle surrounding the ovary. At 46 MeV, a higher percentage of proton energy is deposited within the tissues compared to higher energies (47 MeV and 48 MeV) for the ovary computation. This means that proton energy between 46 MeV and 48 MeV can be used to treat various types of ovarian tumours. However, it is important to protect the surrounding tissues from collateral damage that may prolong the patient’s recovery period, especially at low energy.

Overall, proton energy within the range of 50 MeV to 89 MeV is useful for treating liver cancer, while proton energy within the range of 46 MeV to 48 MeV is suitable for treating ovarian cancer. Beyond these energy ranges, most of the protons will be completely transmitted through the computation phantom without interacting with the target. Since experimenting with living tissues and organs can be challenging, using a simple theoretical model like the one we use here is essential for studying the energy requirement and dose distribution to be used in proton beam therapy before attempting the real treatment.

**Conflicts of interest:** The authors declare no conflict of interest nor any competing interest in the manuscript.

**Acknowledgement:** We acknowledge that this research did not receive any specific grants from public, commercial, or not-for-profit sectors.

**References**


