Evaluating the effect of nuclear interactions on proton dose distributions through convolution methods

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by

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Abstract

Cancer is a disease that causes almost 10 million deaths each year. Currently, there is no perfect treatment for it. However, there is a promising treatment called proton radiotherapy. This works almost the same as one of the older cancer treatments called photon radiotherapy. However, radiotherapy with protons has an advantage in comparison with radiotherapy with photons. This advantage lies in the way the protons lose their energy when going through tissue. The protons deliver most of their dose in a very small region. Cause of this advantage, proton radiotherapy can deliver a lot of dose into the tumour while minimizing the dose delivered into healthy tissue. But this advantage can change into a disadvantage when the location of the tumour moves a few millimeters.
Therefore ideally a scan is taken each time the patient comes in, so the location of the tumour is known very accurately. After the scan it is best to immediately create a treatment plan and do the treatment session. But creating a treatment plan takes to much time to be able to do that. Mainly, this is because the calculation of the dose distribution is not fast enough. This report studies a faster method for the calculation of the dose distribution. The method is derived by the Medical Physics & Technology group from TU Delft. This method is currently not accurate enough to use for treatment planning. The problem of the method is that the dose due to nuclear interactions is not included correctly. The goal of this report is to make the method more accurate by adding the nuclear dose caused by secondary particles formed due to inelastic nuclear interactions to the dose calculated by the existing method.
The nuclear dose is calculated using a convolution of a kernel with the proton flux. The nuclear dose of the following secondary particles is calculated: alpha particles, deuteron particles and secondary protons. Adding the nuclear dose caused by these three secondary particles increased the accuracy of the model by 0.36 percent. However adding the nuclear dose calculation increased the time needed to calculate the dose distribution with 18625 percent. By calculating the convolution using the fast Fourier transform this could be decreased by a factor of 11. However adding the nuclear dose calculation to the fast method increases the time needed to calculate the dose distribution too much. Therefore the calculation of the dose distribution is not fast enough to scan a patient and immediately start with the best possible treatment plan using the fast method with the nuclear dose calculation added.

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Contents

1 Introduction

Cancer is a disease that is caused when cells in your body are replicating uncontrollably fast and grow outside their usual boundaries. These cells are named tumour cells and a lot off tumour cells together are called a tumour. The tumour cells often spread to other parts of the body, this is called metastasis. When this happens, it is very difficult to remove all the tumour cells from a patient's body. According to the WHO, the world health organisation, cancer takes almost 10 million lives each year and with that number it was one of the leading causes of deaths in 2020 [1].

1.1. Cancer treatment

There are different treatments when a patient is diagnosed with cancer. Some of the methods that are frequently used for cancer treatment are surgery, chemotherapy and radiation therapy. This study is focused on one particular type of radiation therapy namely, proton therapy.

1.1.1. Proton radiotherapy

Working of proton radiotherapy

Radiation therapy, also called radiotherapy, is a therapy which uses ionizing radiation to kill the tumour cells. The ionizing radiation can be divided into two parts. At the one side there are the electromagnetic waves, for example X-rays or gamma rays, at the other side there are particles, for example protons or alpha particles. In the case of proton radiotherapy, the ionizing radiation used is a beam of high energetic protons. When travelling through tissue the protons collide with atoms of that tissue. During the collisions energy is transferred from the protons to the atom, slowing down the protons itself and ionizing the atoms. The energy delivered from the radiation to the tissue is called the absorbed dose. The ionization of atoms inside the cell will frequently damage the DNA. When the DNA of a cell is damaged, the cell loses some cell functions, like its ability to divide. [2] The downside of radiation therapy is that healthy cells are also affected by the radiation. Therefore, you want to deliver the dose very accurately inside the tumor and not in the healthy tissue. It can be seen from figure 1.1 that protons are very promising to use for radiotherapy instead of X-rays. X-rays deliver the highest dose in the entry region of the patient while protons deliver the highest dose further in the patient. The peak of the dose distribution for protons is called the Bragg peak. The distance of the Bragg peak is dependent on the energy of the proton. The Bragg peak for a single proton is very narrow, but when protons with a range of energies are used it results in a spread out Bragg peak. Because protons deliver most of their dose in a small region, proton therapy is more prone to little movements than radiation therapy with X-rays.

Treatment planning

Because healthy tissue is also affected by radiation, it is necessary to carefully plan a treatment to deliver the least dose as possible in the healthy cells, while delivering enough dose in the tumour cells to destroy them. A patient usually undergo proton therapy for 5 days to several weeks and the number of therapy sessions differs from 5 to 39. [3] A patients anatomy differs every new therapy session. Because the Bragg peak is usually a few millimeters wide [4] a small change in tumour position, due to

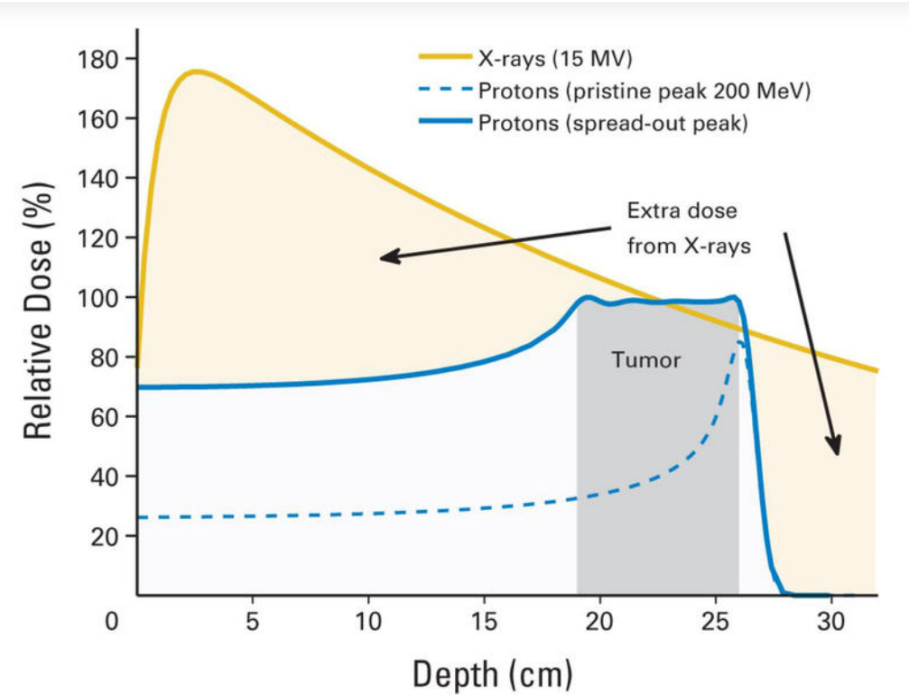

Figure 1.1: The dose distribution of X-rays and protons. In this figure you can see that in theory proton radiation therapy delivers less dose to healthy cells than X-ray radiation therapy. Figure from [5]

for example a fuller stomach of the patient then before, can have a big impact on the dose distribution. Therefore, it would be best to scan the patient each new therapy session and immediately calculate the treatment plan, because then the location of the tumour can not have changed very much. Currently creating a good treatment plan costs much computer power [6] and therefore the treatment planning takes to much time to begin the newly calculated therapy session immediately after a scan. That is why there should be a faster treatment planning system (TPS). A TPS is a tool to optimize the treatment plan for a patient. A TPS calculates many dose distributions every time it optimizes a treatment plan. [6] These dose calculations are mostly done with the Monte Carlo method, which is very accurate, but also slow. There are faster methods already, but these are not as accurate as the Monte Carlo method. This study tries to improve the accuracy of a fast dose calculation method, a previously written algorithm done by the Medical Physics & Technology group form TU Delft. [7] The goal for this report is to make the dose calculation of the previously written algorithm accurate enough to use in treatment planning systems to make the treatment planning fast enough to be able to scan a patient and immediately treat the patient with the best treatment plan possible.

1.2. Outline of thesis

In this report a quick algorithm for the dose calculation is discussed and the goal is to make it more accurate. This method of dose calculation is very fast but less accurate than the Monte Carlo method. This is partly because the method does not take inelastic nuclear interactions into account. This thesis aims to add the dose resulting from these nuclear interactions into the current algorithm to make the method more accurate. Both the Monte Carlo method and the current algorithm are described in chapter 2 together with the proton interactions and the convolution. Chapter 3 covers the method of adding the inelastic nuclear dose to the algorithm and it covers the optimization method. After the optimization is discussed the results of this optimization are discussed in chapter 4. An analysis of the accuracy and the computational efficiency of the new method is given in chapter 5. Finally the conclusion and recommendations for further research are being treated in chapter 6.

2

Proton transport and convolution theory

2.1. Proton interactions with tissue

When protons are traveling through tissue there are multiple different interactions that can occur. The most probable interactions can be classified into three groups: elastic interactions, inelastic electron interactions and the inelastic nuclear interactions.[8] In elastic interactions the kinetic energy is conserved, but in inelastic interactions it is not.

2.1.1. Elastic interactions with nucleus

The protons interact with the nucleus through Coulomb forces. Therefore this type of reactions is also called Coulomb scattering. The Coulomb force is a force between two charged particles. In this case it is a repelling force between the nucleus and the proton because they both have a positive charge. Figure 2.1 show the change in direction of the proton caused by the elastic interactions. The energy loss of the protons due to the elastic interactions is very small in comparison with the inelastic nuclear interactions and therefore the energy loss is negligible. [8]

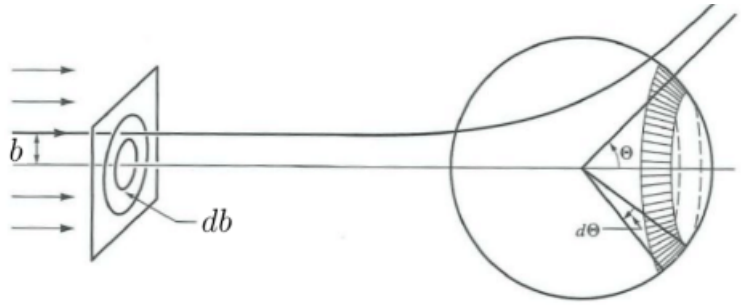

Figure 2.1: This figure shows the trajectory of a proton which interact elastically with the nucleus through the Coulomb force. b is called the impact parameter and Θ is the change in direction of the proton. Figure from [8]

2.1.2. Inelastic electron interactions

The same as with the nucleus the protons interacts with the electrons of the atoms through Coulomb forces. The protons and electrons have a opposite charge and therefore they attract each other. The electrons are way lighter than the nucleus and therefore the change in direction of the proton due to the Coulomb forces with the electrons are negligible. However the energy loss of the protons due to the inelastic electron interactions is big in comparison with the elastic interactions with the nucleus. [8]

2.1.3. Inelastic nuclear interactions

Inelastic interactions are nonelastic collisions where the proton penetrates the nucleus interacting with the individual particles of the nucleus. [8] During the penetration the incident proton can be absorbed

by the nucleus and other particles can be created. The particles that are created due to the inelastic nuclear interactions are called secondary particles. Some possible secondary particles are protons, neutrons and alpha particles. The secondary particles can contribute to the dose. The dose due to the secondary particles is called the nuclear dose. The most probable secondary particles to be formed due to the primary protons are: protons, neutrons, gammas, deuterons, He3's, and alpha's. [9] Therefore these are the secondary particles that are considered in this report.

2.2. Dose calculation

Making a good treatment plan is very important for the patient. There are a lot of variables in the treatment plan for each treatment such as the number of protons, the place where the protons are aimed and the entrance angle of the beam protons. To get the best options for the different variables there has to be a scan of the patient first. From that scan the locations of the tumour and all the organs are known. Then absorbed dose inside the tumour is optimized, while minimizing the dose in healthy tissue. There have to be done a lot of dose calculations to optimize the treatment plan. In chapter 1 was mentioned that ideally a scan is taken each time and then a treatment plan is calculated immediately. This is important because the proton dose distribution has a region of a few millimeters where it delivers the most dose and shortly after that region they do not deliver dose anymore. If the location of the tumour is only known before the first therapy session it can be that after one week no dose is delivered to the tumour, because the tumour is moved a few millimeters deeper inside the patient. During a scan the patient is also exposed to radiation, but the extra absorbed dose in the healthy tissue due to the scan is less then if the Bragg peak of the dose distribution is inside the healthy tissue due to a movement of the tumour. Not all dose calculation methods are fast enough to take a scan every treatment session and calculate the best treatment plan to immediately start the treatment session. There are a lot of different methods to calculate the absorbed dose. The method that is currently the golden standard for proton therapy treatment planning is the Monte Carlo method, but the downside of this method is that it is very slow.

2.2.1. Monte Carlo method

In proton therapy beams of thousands of protons are used. The Monte Carlo method tracks the trajectory for every single proton. The Monte Carlo method is the most accurate method for simulating particle interactions within a medium. It tracks the trajectories of protons in very small steps and for each step it randomly samples from probability distributions. [10] The probability distributions contain the probability for different interactions to happen based on the current energy and direction of the proton. The chance for a certain interaction to happen is called the cross section. The cross section is defined as the number of particles scattered per unit of length divided by the number of incident particles.

2.2.2. Current algorithm

To calculate the dose distribution the proton flux is needed. The movement of protons can be described by the linear Boltzmann equation derived by Dudderstadt and Hamilton [11]. The linear Boltzmann equation is an exact equation for the proton flux. Equation 2.1 is the linear Boltzmann equation.

$$\hat{\Omega} \cdot \nabla\phi(\vec{r}, E, \hat{\Omega}) + \sigma_t \phi(\vec{r}, E, \hat{\Omega}) = \int_{4\pi} \int_0^\infty dE' \sigma_s(\vec{r}, E' \rightarrow E, \hat{\Omega}' \rightarrow \hat{\Omega}) \phi(\vec{r}, E', \hat{\Omega}') d\hat{\Omega}' \tag{2.1}$$

$\hat{\Omega}$ is the direction of a particle, E is the energy of a particle, $\vec{r}$ is the place of a particle. ϕ is the flux. Here σ_t and σ_s are cross sections. σ_t is the total cross section and σ_s is the total scatter cross section. By using multiple approximations the linear Boltzmann equation is derived into two partial equations, The Fokker-Planck equation and the Fermi-Eyges equation. This derivation is done by Burlacu [12] and Asadzadeh [12]. The derivation of the linear Boltzmann equation leads to equation 2.2.

$$\phi(x, y, z) = \int_{4\pi} \phi_{FE}(x, y, z, \Omega_x, \Omega_y) d\vec{\Omega} \cdot \int_0^\infty \phi_{FP}(z, E) dE \tag{2.2}$$

Here ϕ is the proton flux, ϕ_{FE} is the Fermi Eyges flux and ϕ_{FP} is the Fokker-Planck flux. The Fokker-Planck flux is the solution of the Fokker-Planck equation. Equation 2.3 is the Fokker-Planck equation.

$$\frac{\partial}{\partial x}\phi_{FP} = \frac{\partial}{\partial E}S\phi_{FP} + \frac{1}{2}\frac{\partial^2}{\partial E^2}T\phi_{FP} \tag{2.3}$$

ϕ_{FP} is the Fokker Planck flux, S is called the stopping power coefficient and T is called the energy straggling coefficient. The algorithm solves the Fokker-Plank equation numerically using the Discontinuous Galerkin method.
The first term of the right hand side of equation 2.2 can be calculated using equation 2.4.

$$\int_{4\pi} \phi_{FE}(x, y, z, \Omega_x, \Omega_y) d\vec{\Omega} = \frac{A^2}{2\pi\xi^2(z)} exp\left(-\frac{x^2 + y^2}{2\xi^2(z)}\right) \tag{2.4}$$

A and ξ are coefficients of the Fermi Eyges solution.

The algorithm is a very fast method in comparison with the Monte Carlo method, however it is less accurate than the Monte Carlo method and not accurate enough to use in proton therapy dose calculations. The algorithm does take inelastic nuclear interactions into account, but only the locally dose delivered by the secondary particles. While secondary particles coming from the inelastic nuclear interactions can also deliver much dose further from the interaction place [9].

2.3. Convolution

Mathematically a convolution is an operation that calculates the amount of overlap of one function, usually called the kernel, that is shifted over another function. For discrete functions the convolution is calculated by shifting the kernel over the data and for each shift do a element wise multiplication and put the result in the place corresponding to the shift of the kernel. The formula for the convolution between two 1D arrays u and v is shown in equation 2.5.

$$(u \otimes v)(k) = \sum_i u(i)v(k - i) \tag{2.5}$$

An example of discrete convolution with two 1D arrays is shown in figure 2.2.

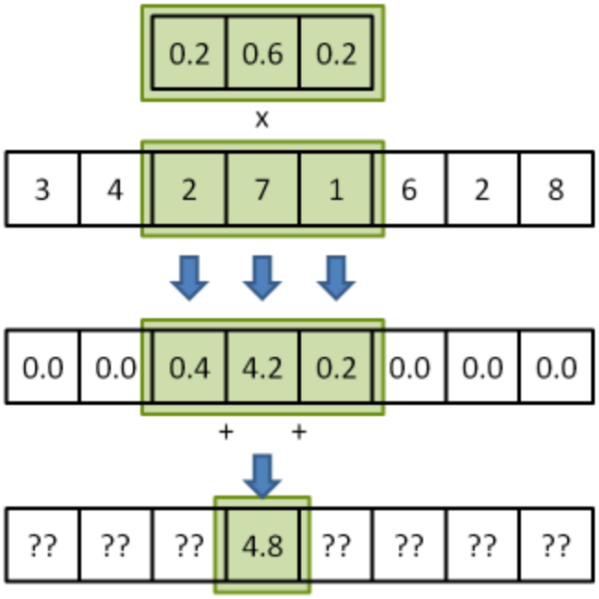

Figure 2.2: Convolution of two 1D arrays. Figure from [14].

3

Nuclear dose calculation

3.1. Nuclear dose calculation using a convolution

For the calculation of the nuclear dose a convolution method is used. The calculated nuclear dose is calculated as the convolution between the proton flux and a kernel. For the absorbed nuclear dose the Monte Carlo (MC) dose is used, because this dose is seen as the golden standard. All types of secondary particles have a different nuclear dose distribution. Therefore for each different particle a different kernel should be used. To get the correct result the Monte Carlo nuclear dose is found for each different particle. Equation 3.1 shows the nuclear dose calculation for one type of particles using a convolution.

$$D_{conv}(i,j,k) = (\phi \otimes k(\vec{\theta}))(i,j,k) = \sum_{l}\sum_{m}\sum_{n} \phi(l,m,n)k(i-l,j-m,k-n) \tag{3.1}$$

Where ϕ is the proton flux, k is the kernel, $\vec{\theta}$ is the vector containing the kernel parameters and D_{conv} is the dose from the convolution.

3.1.1. Data collection

To find the kernel for which the nuclear dose following from the convolution is as close as possible to the Monte Carlo nuclear dose the following data is needed: The Monte Carlo dose, the proton flux and the kernel. The Monte Carlo dose and the proton flux is data that can be collected from simulations. The proton flux and the Monte Carlo dose is taken for a incoming 100 MeV proton beam. There is also a energy straggling included. This means that all the protons in the beam start within an energy range around 100 MeV. Everywhere in this report this proton beam energy is used.
The dose and the proton flux are dependent on the medium of propagation. In this report water is used as medium. This reflects tissue from a patient well, because the most atoms in a patients tissue are water atoms. For the data collection a water tank of 5 cm by 5 cm in lateral direction and 10 cm in depth direction is used. The water tank is divided into voxels of 0.1 cm x 0.1 cm x 0.01 cm.

Monte Carlo dose

In section 2.2 the most probable secondary particles that give secondary dose are listed. The nuclear secondary dose for all this particles is collected using a Monte Carlo dose calculation code called TOPAS [15]. TOPAS has possibilities to give a dose result which includes only the particular dose that is wanted. The absorbed dose for all the different secondary particles is calculated using TOPAS. For each particle type it gives the nuclear dose delivered by that type of particle and the dose delivered by possible tertiary, quaternary, etc. particles that deliver dose.

Flux

The proton flux is calculated in the code to find the dose distribution. Section 2.2.2 describes the calculation of the proton flux. The result is shown in Figure 3.1

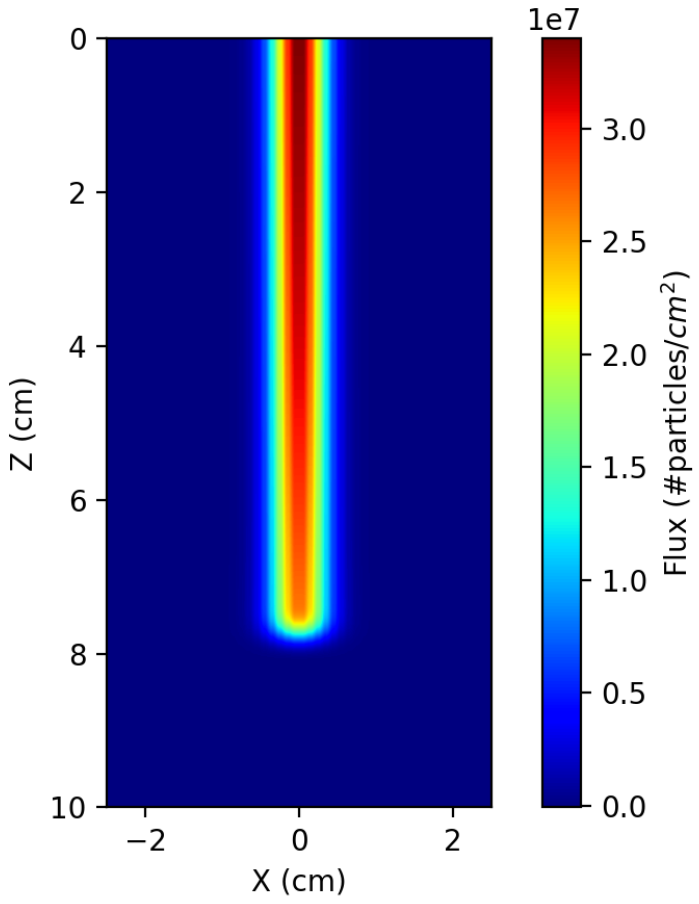

Figure 3.1: A plot of the proton flux for y = 0 cm.

3.2. Kernel shapes and parameters

Figure 3.2 shows the dose per particle for each slice in depth. The figure includes the the primary proton dose and the dose of the possible secondary particles. In Figure 3.2 can be seen that the secondary alpha's, protons and deuterons deliver the most dose of the secondary particles. Because these deliver the most dose, kernels for these particles are created.

3.2.1. Lateral shape

All kernels have the same xy-profile. Found was that a Gaussian shape was a good way to represent the xy-profile of the secondary doses. This is decided by looking at the xy-profile of the dose distribution and fit a Gaussian function on the xy-profiles. The Gaussian function has two parameters for each dimension, σ and μ and these parameters decide the width of the xy-profile and the location of the peak. Because the dose distribution is symmetrical around zero the μ_x and μ_y both should be zero. The remaining Gaussian function is the following,

$$G(x,y) = Aexp\left(-\left(\frac{x^2}{2\sigma_x^2} + \frac{y^2}{2\sigma_y^2}\right)\right) \tag{3.2}$$

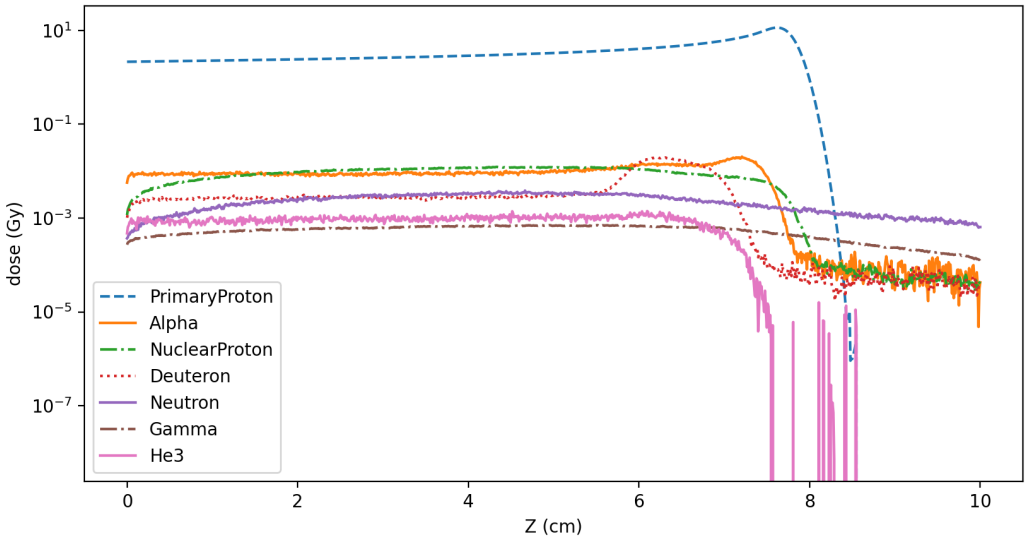

Figure 3.2: A logarithmic plot for the dose per slice in depth of the secondary particles and the primary protons.

Where A is the amplitude and σ_x and σ_y are the parameters which define the width of the Gaussian in respectively the x and the y direction. A, σ_x and σ_y will be parameters of the optimization. The length of the kernel in lateral direction will be taken high. Then when the kernel is created a analyse of the kernel will be done to calculate after which size the kernel value is so low it has almost no impact on the dose distribution.

3.2.2. Depth shape

A kernel can have any shape and therefore it can have a lot of applications. One of the important applications that are used is a shift kernel. That is a kernel which shifts the input data any wanted number of voxels. A shift kernel which shift the proton flux one voxel in depth direction has the following form in the depth direction,

$$K_{shift} = \begin{pmatrix} 1 \\ 0 \\ 0 \end{pmatrix}$$

Another frequently used kernel is the Sobel kernel [16]. The Sobel kernel is used in image filtering as an edge detector. A convolution with the Sobel kernel in depth direction will give a high value where the proton flux is changing fast in depth direction. The Sobel kernel is of the following form in depth direction,

$$S_z = \begin{pmatrix} 1 \\ 0 \\ -1 \end{pmatrix}$$

Alpha dose

The alpha dose is shown in Figure 3.3. The dose distribution has almost the same shape as the Bragg peak of the primary protons. The secondary alpha particles deliver their most dose in the Bragg peak region and that is the region where the proton flux is decreasing quickly. Therefore a Sobel kernel should give a good approximation for the dose distribution of alpha particles in the Bragg peak region. The alpha particles also deliver dose in the entrance region. This is the region from z = 0 until the Bragg peak region. This dose is approximated by using a shift kernel.
So for the alpha particles the kernel will be a combination of a shift kernel with a shifted Sobel kernel. The optimization parameters are the amplitude of the shift kernel (A_{shift}), the distance of the shift, the amplitude of the Sobel kernel (A_{Sobel}) and the shift of the Sobel kernel.

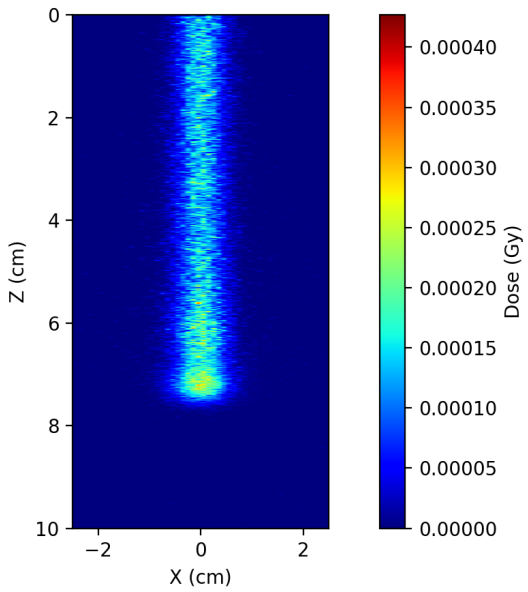

Figure 3.3: Alpha dose distribution for y = 0 cm.

Deuteron dose

The deuteron dose is shown in Figure 3.4. In the deuteron dose distribution there is a peak just before

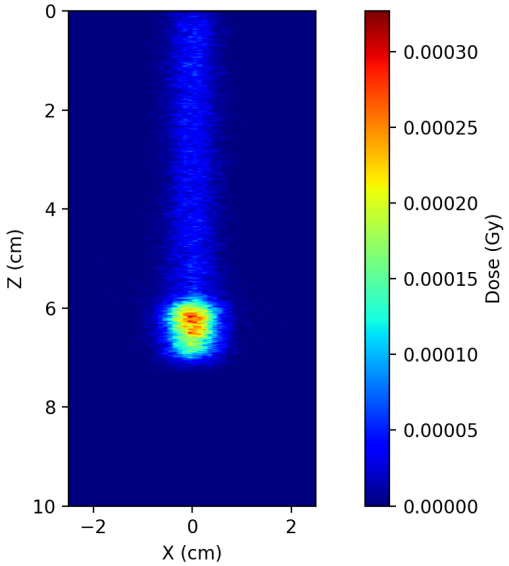

Figure 3.4: Deuteron dose for y = 0 cm.

the Bragg peak region. The peak of the deuteron dose distribution is more spread-out in the depth direction then the peak of the alpha dose ditribution. Therefore multiple shifted Sobel kernel are used. There is also another kernel shape which is used, namely the Prewitt kernel [17]. The Prewitt kernel is also used for edge detection and is of the form,

$$K_{Prewitt} = \begin{pmatrix} 2 \\ 1 \\ 0 \\ -1 \\ -2 \end{pmatrix}$$

To account for the entrance dose of the deuteron dose distribution a shift kernel is used.
The kernel for the deuteron dose calculation will be a combination of a shift kernel with multiple shifted Sobel kernels and shifted Prewitt kernels. The parameters of this kernel are the shift distance, the shift for each Sobel kernel, the amplitude of each Sobel kernel, the shift for each Prewitt kernel and the amplitude for each Prewitt kernel.

Nuclear proton dose

The nuclear proton dose is shown in Figure 3.5. In comparison with the deuteron dose the nuclear

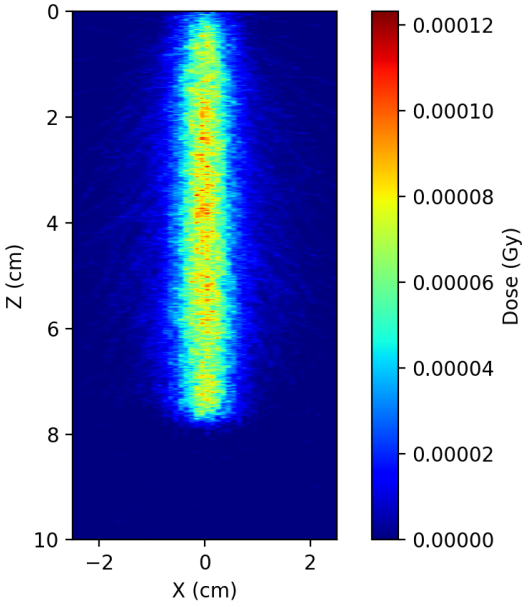

Figure 3.5: Nuclear proton dose for y = 0 cm.

proton dose distribution has more dose in the entrance region and less in the Bragg peak region. The dose distribution is almost constant in depth direction. Therefore the used kernel for the nuclear proton dose is a combination of multiple shift kernels. Multiple shift kernels are used to account for the fact that the dose distribution does not have exactly the same shape as the proton flux. The parameters of this kernel are the amplitude and the shift distance for every shift kernel.

3.3. Optimization

To get the best dose calculation as possible from the convolution the kernel should be optimized. The most important part of the optimization is the kernel shape. The kernel shapes are discussed in section 3.2. In this study the best kernel is defined as the one which results in the least sum of squared error (SSE). The SSE is the sum over all the voxels of the squared difference between the Monte Carlo dose and the dose from the convolution. The function for the SSE, which is going to be minimized, is the following,

$$\sum_{i,j,k}(D_{conv}(i,j,k) - D_{MC}(i,j,k))^2 = \sum_{i,j,k}((\phi \otimes k(\vec{\theta}))(i,j,k) - D_{MC}(i,j,k))^2 \tag{3.3}$$

where D_{conv} is the dose from the convolution of the kernel with the proton flux, D_{MC} is the dose from the Monte Carlo method, ϕ is the proton flux, k is the kernel and $\vec{\theta}$ is the vector containing the kernel parameters. The goal of the optimization is to find the $\vec{\theta}$ which minimizes the SSE.
The function used to minimize the SSE is: $scipy.optimize.fmin$ [18]. This is a function of the SciPy module [19] and it minimizes a function using the downhill simplex algorithm. [20]
For each different secondary particle an optimization was done using its kernel shape and parameters. For the optimization a kernel of the same size of the proton flux was used. The function

$scipy.optimize.fmin$ gave the optimized value of the parameters and the function value for the best parameter values. Then the kernel was plotted and the kernel was downsized where it could. This means that all the zero values at the edges were removed and that the lateral size of the kernel stopped where the kernel value was less than $1e^{-}3$ times the middle of the kernel. A check of the parameters was done after the optimization to make sure that all the parameters were possible and to make sure if the dose from the convolution was of the shape as the Monte Carlo dose.

4

Results

4.1. Kernel parameters

4.1.1. Lateral kernel parameters

The kernel parameters in lateral direction are the same parameters for all three kernels. They are the parameters of the Gaussian function, namely σ_x and σ_y. The optimized results for these parameters are showed in the Table 4.1.

	Alpha kernel	Deuteron kernel	Nuclear proton kernel
σ_x	0.2 cm	0.19 cm	0.34 cm
σ_y	0.2 cm	0.12 cm	0.24 cm

Table 4.1: Optimized parameters for the kernels in lateral direction.

4.1.2. Depth kernel parameters

The depth kernel parameters are the amplitudes and the shifts of the multiple basic kernels. All the shift distances are negative, this means that they all shift the proton flux in the negative z direction, so they make the dose come less deep inside the medium.

Alpha dose

After the optimization the alpha dose kernel was a combination of the shift kernel and the Prewitt kernel. The returned parameters are stated in Table 4.2.

	Prewitt kernel	Shift kernel
A	$1.2e^{-12}$	$-2.4e^{-13}$
Δz	-0.48 cm	-0.43 cm

Table 4.2: Optimized parameters for the Alpha kernel.

Where A is the amplitude for the given kernel and Δz is the shift distance into the positive z direction. The SSE with these parameters is $1.43e^{-4} Gy^2$. The resulting kernel is shown in figure 4.1.

Deuteron dose

After the optimization the deuteron dose kernel was a combination of three Sobel kernels, one Prewitt kernel and one shift kernel. It consisted of two more Prewitt kernels, but there amplitude was less than $1e^{-3}$ times the other lowest amplitude. Therefore the extra two Prewitt kernels are neglected. The returned parameters are stated in Table 4.3.
A and Δz are respectively the amplitude of kernels and the shift distance in the positive z direction. The SSE with these parameters is $3.34e^{-5} Gy^2$. The resulting kernel is shown in figure 4.2.

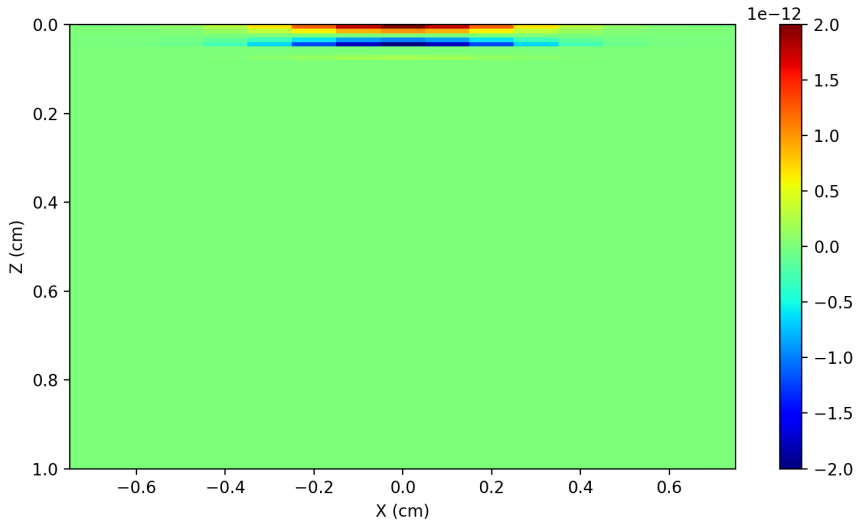

Figure 4.1: Middle slice of the kernel for the secondary alpha dose.

	Prewitt kernel	Sobel kernel 1	Sobel kernel 2	Sobel kernel 3	Shift kernel
A	$3e^{-12}$	$6e^{-12}$	$3e^{-12}$	$2e^{-12}$	$1.6e^{-13}$
Δz	-1.73 cm	-1.43 cm	-1.13 cm	-0.98 cm	-1.75 cm

Table 4.3: Optimized parameters for the Deuteron kernel.

Nuclear proton dose

After the optimization the proton dose kernel was a shift kernel. The parameters found are in Table 4.4.

	Shift kernel
A	$1.64e^{-14}$
Δz	-0.05 cm

Table 4.4: Optimized parameters for the nuclear proton kernel.

The SSE with these parameters is $2.27e^{-5}Gy^2$. The resulting kernel is shown in figure 4.3.

4.2. Dose from convolutions

The secondary alpha dose calculated by doing a convolution of the alpha kernel with the proton flux is shown in Figure 4.4. The secondary deuteron dose calculated by doing a convolution of the deuteron kernel with the proton flux is shown in Figure 4.5. The Nuclear proton dose calculated by doing a convolution of the nuclear proton kernel with the proton flux is shown in Figure 4.6.
The total nuclear dose distribution is shown in Figure 4.7. The most nuclear dose is inside the Bragg peak region. This can also be seen from Figure 4.8.

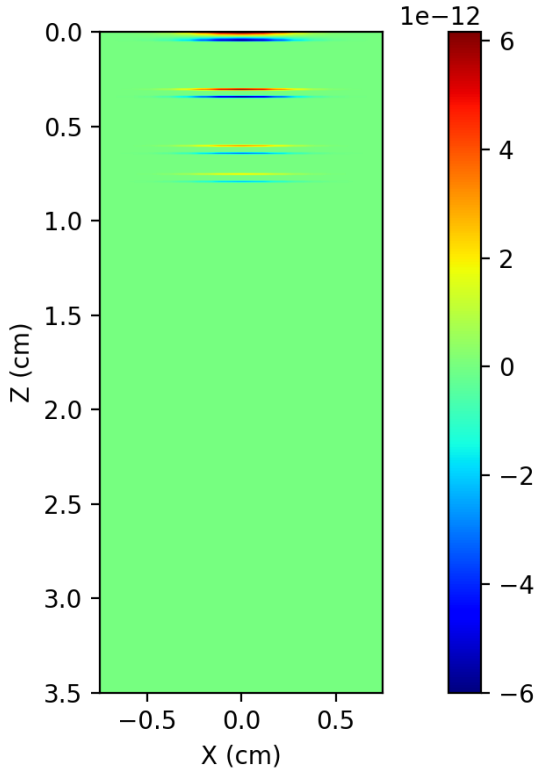

Figure 4.2: Middle slice of the kernel for the secondary deuteron dose.

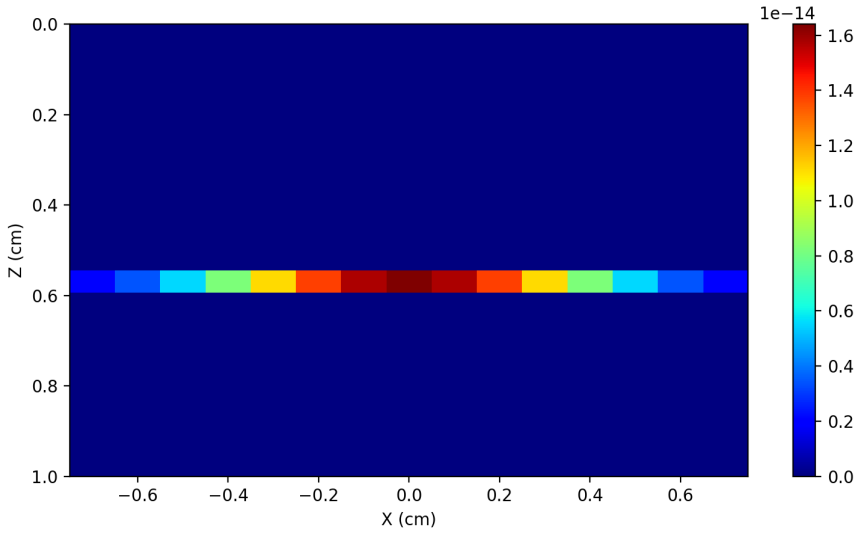

Figure 4.3: Middle slice of the kernel for the nuclear proton dose.

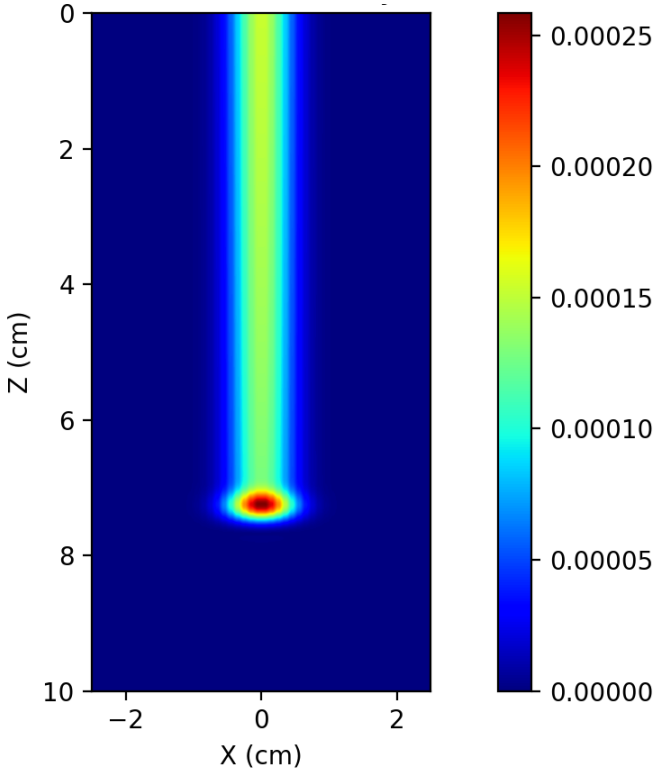

Figure 4.4: Secondary alpha dose distribution. Result of the convolution of the alpha kernel with the proton flux.

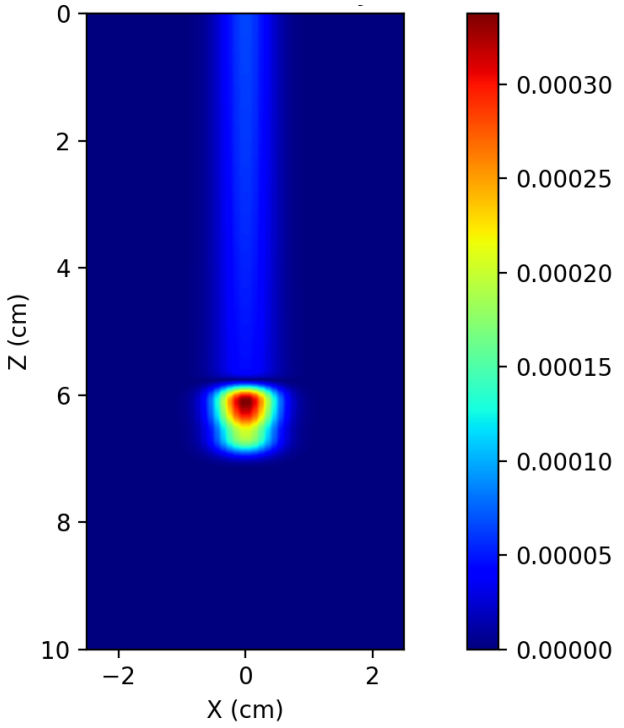

Figure 4.5: Secondary deuteron dose distribution. Result of the convolution of the alpha kernel with the proton flux.

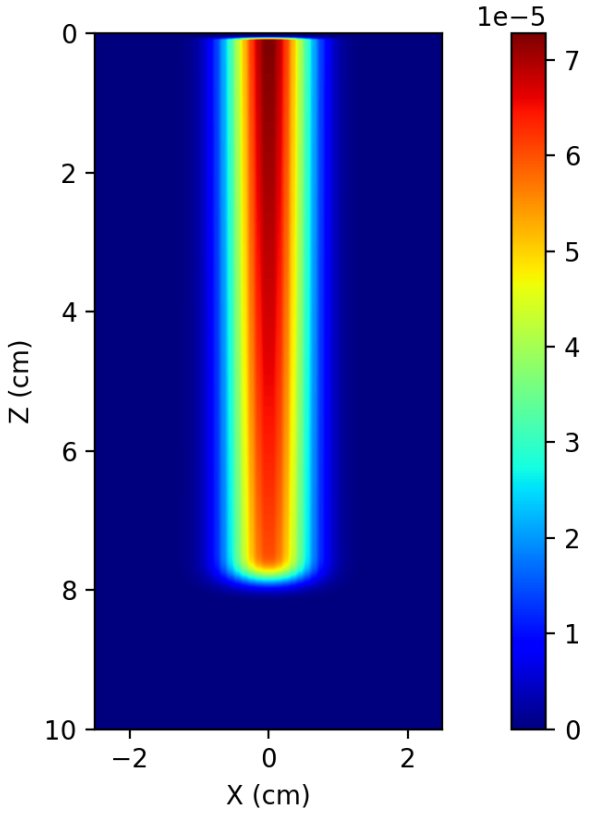

Figure 4.6: Nuclear proton dose distribution. Result of the convolution of the nuclear proton kernel with the proton flux.

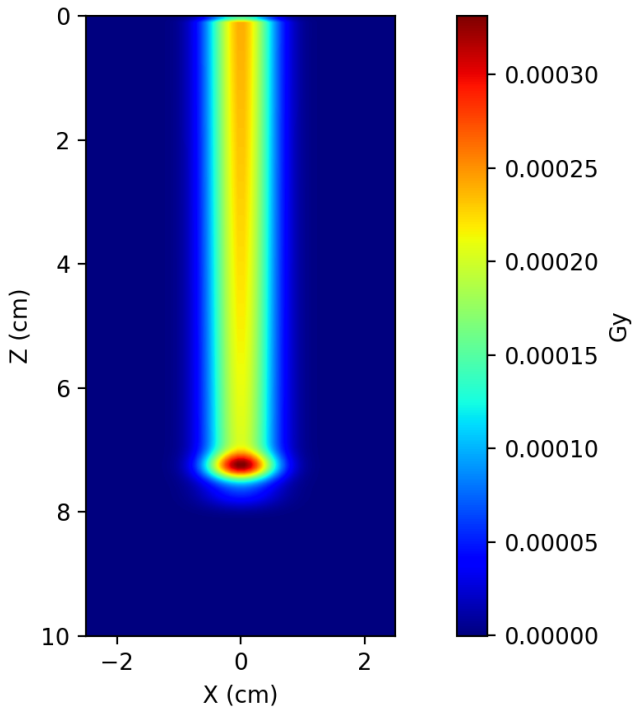

Figure 4.7: Total nuclear dose distribution for y = 0 cm.

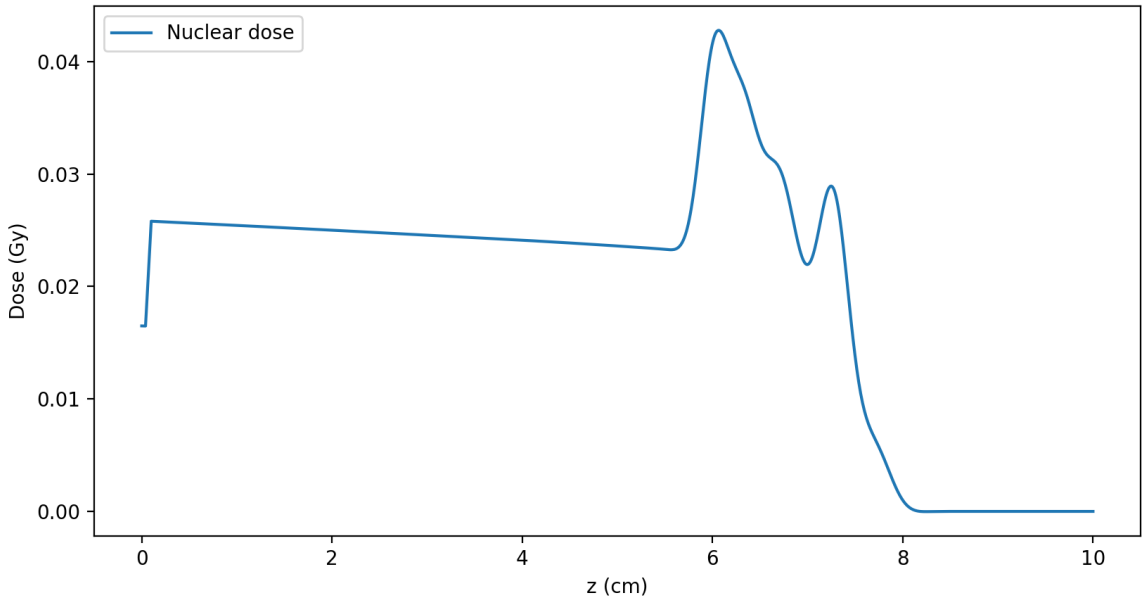

Figure 4.8: Total nuclear 1D dose distribution. The slice dose is the summation of the dose over all the voxels inside that slice

5

Model accuracy and computational efficiency

5.1. Model accuracy

The measurement of the model accuracy is done by calculating the sum of squared errors (SSE). The SSE is calculated by summing the squared difference of the dose from the convolution and the dose from Monte Carlo of each voxel. The SSE for the algorithm without adding nuclear dose is 6.828. Adding the nuclear dose to the algorithm decreased the SSE, and therefore increased the accuracy, by 0.36 percent.
Another widely used measure is the integral depth dose (IDD). The IDD is obtained by integrating the dose in each depth slice. This measure is a way to visualize a 3D data array into a 2D plot. Therefore the IDD makes it easier to see what exactly is the difference between different dose distribution. In figure 5.1 the IDD of the current algorithm with and without nuclear dose and that of the Monte Carlo dose distribution are shown.

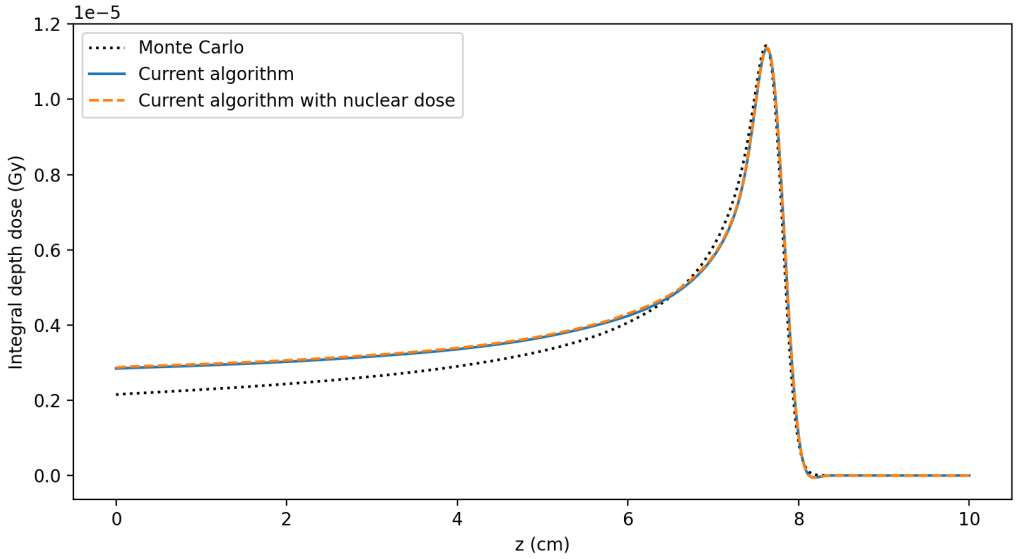

Figure 5.1: A plot of the integral depth dose for the Monte Carlo method and the current algorithm with and without nuclear dose.

To compare the current algorithm with and without nuclear dose the SSE of the IDD is taken. The SSE is calculated by summing the squared difference between the slice dose from the convolution and the slice dose from Monte Carlo for all slice. The SSE of the integral depth dose for the algorithm without

the nuclear dose added is $1.84e^{-10}$. Adding the nuclear dose increased the SSE with 11.71 percent. Figure 5.2 show the squared difference for each slice in depth.

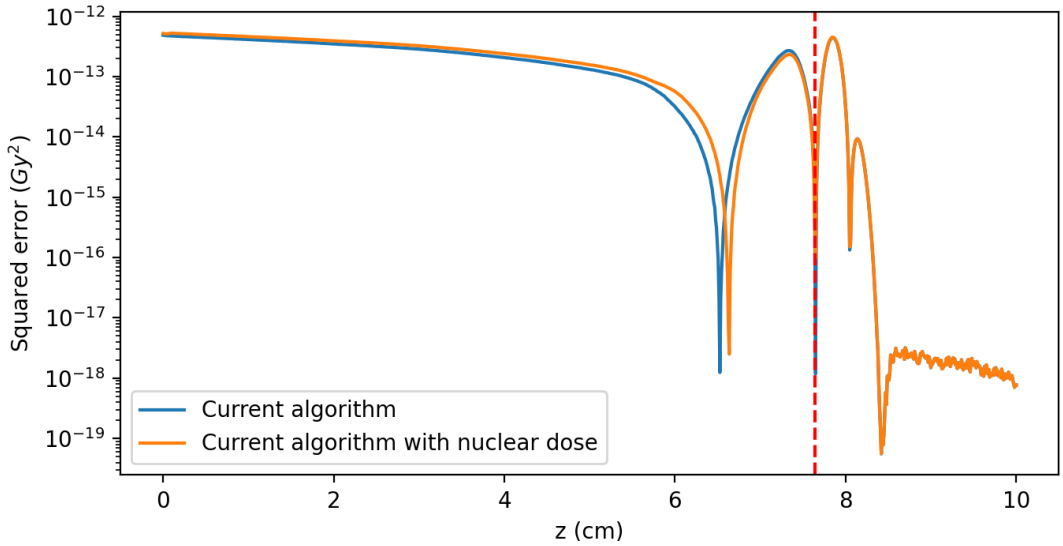

Figure 5.2: Plot of the squared error between the current algorithm with or without nuclear integral depth dose and the Monte Carlo integral depth dose. The red vertical line is the Bragg peak distance

From Figure 5.2 can be seen that there is first a large region where adding the nuclear dose decreased the accuracy of the model. After that there is a small region where The accuracy is improved, this region is just before the Bragg peak.

5.2. Computational efficiency

The dose calculations are done on a regular laptop using the GNU fortran compiler [21]. The number of protons used in the calculations is $2e^{-7}$. The algorithm takes on average 8 seconds to calculate the dose distribution. The nuclear dose calculation takes on average 300 seconds for the alpha dose and for the nuclear proton dose and 890 seconds for the deuteron dose. The deuteron dose calculation takes almost 3 times as long as the other two nuclear doses because the kernel for the deuteron dose is 3 times as long. By adding the nuclear dose to the code the time needed to calculate the dose distribution is increased with 18625 percent. A lot of the extra time comes from the fact that the convolution is calculated directly. This direct calculation is very computational inefficient. Another way to calculate an convolution is using the fast Fourier transform (FFT). Using the FFT to calculate a convolution is minimal 11 times as fast. [22] If the FFT method is implemented and it is 11 times as fast the nuclear dose calculation will increase the calculation time by 1693 percent. Which is still a big time increase, especially because multiple dose calculation have to be done to make a good treatment plan. However, in comparison with the Monte Carlo dose calculation, which takes around 8 hours on a high performance computing cluster [23], the algorithm with nuclear interactions included is still a fast method.

6

Conclusion and recommendations

6.1. Conclusion

From figure 5.2 can be seen that the nuclear dose added with a convolution is increasing the accuracy for some regions, but decreasing the accuracy for other regions. Adding the inelastic nuclear dose calculation into the algorithm increased the accuracy of the dose calculation by 0.36 percent. However the dose calculation takes at least 1693 percent more time when adding the nuclear dose. Because of that time increase the goal set for this algorithm, to be able to scan a patient, immediately plan the best treatment and start with that treatment can not be achieved.

6.2. Recommendations

The first recommendation for further research is to add the nuclear dose for the other secondary particles too, so for the neutron, gamma, and he-3 particle and see if they increase the accuracy.
In this report the convolution for the dose calculation is calculated in a direct way. There are faster methods like the fast Fourier transform (FFT) method. The FFT method is at least 11 times faster than direct convolution. [22] Therefore a recommendation for further work is to calculate the convolution using the FFT or another fast method. Although, just using the FFT instead of the direct convolution for the dose calculation would be still not fast enough for the goal set for this algorithm. Therefore a another recommendation will be to try optimizing the dose from the convolution for secondary particles with smaller kernels. The accuracy of the optimization will probably be lower, but maybe the accuracy is good enough to still get an increase in model accuracy, while keeping the time cost low enough to be able to achieve the goal for this algorithm.
The last recommendation is to analyse at which range in depth the addition of the nuclear dose increased the accuracy and try to optimize the nuclear dose especially for that range in depths.

7

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