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Bragg peak prediction from quantitative proton computed tomography using different path estimates

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Abstract

This paper characterizes the performance of the straight-line path (SLP) and cubic spline path (CSP) as path estimates used in reconstruction of proton computed tomography (pCT). The GEANT4 Monte Carlo simulation toolkit is employed to simulate the imaging phantom and proton projections. SLP, CSP and the most-probable path (MPP) are constructed based on the entrance and exit information of each proton. The physical deviations of SLP, CSP and MPP from the real path are calculated. Using a conditional proton path probability map, the relative probability of SLP, CSP and MPP are calculated and compared. The depth dose and Bragg peak are predicted on the pCT images reconstructed using SLP, CSP, and MPP and compared with the simulation result. The root-mean-square physical deviations and the cumulative distribution of the physical deviations show that the performance of CSP is comparable to MPP while SLP is slightly inferior. About 90% of the SLP pixels and 99% of the CSP pixels lie in the 99% relative probability envelope of the MPP. Even at an imaging dose of ~0.1 mGy the proton Bragg peak for a given incoming energy can be predicted on the pCT image reconstructed using SLP, CSP, or MPP with 1 mm accuracy. This study shows that SLP and CSP, like MPP, are adequate path estimates for pCT reconstruction, and therefore can be chosen as the path estimation method for pCT reconstruction, which can aid the treatment planning and range prediction of proton radiation therapy.

1. Introduction

An important aspect of treatment planning for proton therapy is to accurately predict the Bragg peak location within the patient for an incoming proton beam of known energy, or equivalently, to find the correct incoming energy for an intended Bragg peak location. To accomplish this, an image set of the anatomy of interest containing electron densities or stopping powers should be known. Currently such an electron density image is obtained by the calibration and conversion of an x-ray computed tomography (CT) image (Mustafa and Jackson 1983, Schneider *et al* 1996, Schaffner and Pedroni 1998). It has, however, been

pointed out that this method can induce up to 2% proton range error (Schaffner and Pedroni 1998), which could substantially limit the benefit of proton therapy. This being one of the larger uncertainties for proton therapy delivery, it requires a more accurate way of acquiring an electron density image or proton stopping power image, and proton computed tomography (pCT) is a potential candidate for accomplishing this.

In the pCT reconstruction scheme proposed by Schulte *et al* (2004), the path of each individual proton needs to be estimated to perform the path integral. Li *et al* (2006) have shown that the straight-line path (SLP), cubic spline path (CSP), and the most-likely path (MLP) are three possible path estimates, and reconstruction using MLP yields an image that has the highest spatial resolution. The MLP estimation was first introduced by Schneider and Pedroni (1994). Later Schulte *et al* (2008) also formulated MLP in the maximum likelihood estimation framework.

Although MLP is the best path estimate among those studied, it is mathematically complicated and computationally costly. Since proton energy uncertainty is the major source of error for quantitative accuracy of pCT reconstruction (Schulte *et al* 2005), the error in the path estimate may not significantly deteriorate the reconstructed pCT image. Hence, the much faster and simpler SLP or CSP may be chosen for pCT reconstruction without significantly compromising image quality. Moreover, until now the effect of using different path estimates for pCT reconstruction on the accuracy of Bragg peak prediction has not been considered. The possibility of accurate Bragg peak prediction is however one of the key utilities of pCT, and one that is more important than the visual quality of the pCT image. Therefore, this paper focuses on accurate Bragg peak location prediction, and characterizes the performance of SLP and CSP compared with the MPP and simulated real path.

Before tackling this question, we would like to consider the purpose of imaging in radiotherapy a bit further. An imaging modality in radiotherapy in general serves two purposes: (1) to show the anatomy of interest, and (2) to provide physical quantities for radiation dosimetry calculations. X-ray CT images serve both purposes: they show the position and size of tumor and normal tissue, and also provide electron densities for treatment planning after calibration and conversion. These two purposes, however, are not necessarily bound together. A certain imaging modality may serve only one purpose and might not serve the other. For example, MR images are helpful in discerning anatomical structures, yet are not useful for dosimetric calculation. On the other hand, an imaging modality may be very useful for dosimetric calculation and be less useful in discerning anatomical structures. pCT fits into this category. When a patient is treated with proton therapy, an x-ray CT image data set or image data sets from other imaging modalities will already have been acquired for treatment target definition. The need for pCT imaging will then solely be for dosimetric purposes. The pCT image should be able to, and only needs to, correctly predict the Bragg peak location for a given incoming proton beam or equivalently find the energy of the incoming beam for an intended Bragg peak location at the time of treatment delivery. Therefore, we will only focus in this study on the quantitative accuracy of pCT images rather than their visual quality, even though pCT can also potentially be a low-dose diagnostic imaging modality.

2. Methods

2.1. GEANT4 Monte Carlo simulation

On a cylindrical phantom with an elliptic base, proton projections were simulated using the GEANT4 simulation toolkit. The cross-section geometry and the densities correspond to the original design of Shepp and Logan (1974). The unit length '1.0', as defined in figure 1 of the paper by Shepp and Logan (1974), is 10 cm in this study, while the length of the cylinder is 5 cm. Therefore, the elliptical cross-section has a major axis of 18.4 cm and minor axis of 13.8 cm. The sizes of other elliptical shapes inside the phantom are scaled accordingly. Material outside the phantom is simulated as air. A virtual sphere with a radius of 12 cm is constructed to surround the phantom in the simulation, hereafter called the reconstruction sphere, yielding a field of view of 24 cm.

A parallel broad 200 MeV proton beam spanning 20 cm that impinges on the phantom has been simulated in 180 view angles with a 2° interval between each view. Since individual proton trajectories are used in algebraic reconstruction, the specific beam geometry is not important for this study. The position and momentum (and thus energy) of each proton at its entrance into and its exit from the reconstruction sphere have been recorded. A maximum step size of 0.5 mm was chosen for the simulation, which is sufficient for a 1 mm × 1 mm pixel size in image reconstruction. The position of each step of the simulated real path is stored and compared to the path estimates. For simulations in water to obtain the physical deviations between path estimates and the real path, a 0.05 mm step size and a 0.1 mm pixel size have been utilized to achieve higher precision.

2.2. Imaging equation and algebraic reconstruction

Using the continuous slowing down approximation (CSDA), we have previously derived the following imaging equation (Wang *et al* 2010):

$$-\int_{E_{\text{entrance}}}^{E_{\text{exit}}} \left[\frac{S}{\rho}(x, y, z) \right]_{E_0}^{E_0} dE = \int_{\text{path}} S(x, y, z, E_0) dl \quad (1)$$

where E_{entrance} and E_{exit} are the proton's kinetic energy when entering and leaving the reconstruction region respectively; E_0 is an arbitrary energy, chosen to be the same as

E_{entrance} in the current study; and $\left[\frac{S}{\rho}(x, y, z) \right]_{E_0}^{E_0}$ is the ratio of mass stopping powers at E_0 and E for the local material at (x, y, z) . As illustrated previously (Wang *et al* 2010),

$\left[\frac{S}{\rho}(x, y, z) \right]_{E_0}^{E_0}$ can be approximated as $\left[\frac{S}{\rho}(\text{H}_2\text{O}) \right]_{E_0}^{E_0}$ with negligible error; therefore, the imaging equation used in this study has the following form:

$$-\int_{E_{\text{entrance}}}^{E_{\text{exit}}} \left[\frac{S}{\rho}(\text{H}_2\text{O}) \right]_{E_0}^{E_0} dE = \int_{\text{path}} S(x, y, z, E_{\text{entrance}}) dl. \quad (2)$$

To apply the path integral to reconstruction of a pixilated image, the next step is to discretize the path integral. This requires explicit knowledge of the path, which can however only be

estimated from the proton's position and direction at the entrance and exit of the reconstruction region.

Discretization of the path integral yields the following imaging equation for an image having a total of N pixels:

$$-\int_{E_{\text{entrance}}}^{E_{\text{exit}}} \left[\frac{S}{\rho}(\text{H}_2\text{O}) \right]_E^{E_{\text{entrance}}} dE \cong \sum_{j=1}^N w_j S_j(E_{\text{entrance}}), \quad (3)$$

where w_j are the weights at each pixel for a given proton ray. Each proton generates one equation of the form given in equation (3), and all of the proton projections taken as a whole yield a set of linear equations for pixel values $\{S_j(E_{\text{entrance}})\}_{j \in \{1, \dots, N\}}$. The simultaneous algebraic reconstruction technique (Andersen and Kak 1984) is used to reconstruct a stopping power image $\{S_j(E_{\text{entrance}})\}_{j \in \{1, \dots, N\}}$ from these imaging equations.

The above imaging equation and reconstruction schema requires knowledge of the position and momentum of each proton at the entrance and exit of the reconstruction region. In this study we assume that we have the means of accurately detecting and measuring these quantities.

2.3. Path estimation methods

In the SLP estimation method a straight line is used to connect the entrance and exit position for each proton; the angular direction of the proton at the entrance and exit is not used. The CSP estimation method uses a third-order polynomial curve fitted from the four detected conditions: entrance position, entrance angular direction, exit position and exit angular direction. On the other hand, in the most-probable path (MPP) estimation method (cf Schneider and Pedroni (1994) and Wang *et al* (2010)) employed in this work, the MPP is extracted from a conditional proton probability map. For a detailed discussion of how such a conditional proton probability map can be obtained using semi-analytical methods, we refer the reader to Wang *et al* (2010).

2.4. Distribution of relative probability and deviation of path estimates

Using the GEANT4 simulated proton path as the real proton path, one can characterize the path estimates described above by comparing their relative probabilities and their deviation from the real path. The conditional proton path probability map is used to obtain the probability of the pixels that lie on the proton paths resulting from the various path estimation methods; from this information a relative probability for each path estimation method is obtained and compared. A cumulative distribution of these relative probabilities is then generated. For deviation from the real path, the distance between pixels resulting from the various path estimation methods and pixels on the real path at the same depth is calculated to yield the deviation from the real path. For the various path estimates, cumulative distributions of the deviation as well as the maximum deviation from the real path for all pixels are then constructed from these data.

2.5. Assessment of quantitative accuracy and Bragg peak location prediction

The average value of the reconstructed stopping powers in each of the major elliptical regions of the simulated phantom is assessed and compared to the actual stopping power for the region, or the ‘ground truth’. As stated above, image noise is not of concern for this study since it focuses on the quantitative accuracy, yet the standard deviation of reconstructed stopping powers in each region is still included for a comparison of image clarity.

The ultimate benchmark of quantitative accuracy is whether the reconstructed image can accurately predict the location of the Bragg peak for a given incoming proton beam of energy E_{entrance} . This is done by a stepwise proton energy and proton energy deposition calculation along its incoming direction on the reconstructed stopping power $\{S_j(E_{\text{entrance}})\}_{j \in \{1, \dots, N\}}$ image. Assume that one has a proton beam with energy E_j that traverses from pixel j into pixel $j+1$ along its path with a step size of d , then the energy deposited in pixel j and the average energy of the proton remaining when entering pixel $j+1$ are respectively

$$\Delta E_j = S_j(E_j) \cdot d \quad (4)$$

$$E_{j+1} = E_j - \Delta E_j, \quad (5)$$

where the stopping power of energy E_j is scaled from the reconstructed stopping power for energy E_{entrance} :

$$S_j(E_j) \cong S_j(E_{\text{entrance}}) \cdot \left[\frac{S}{\rho}(\text{H}_2\text{O}) \right]_{E_{\text{entrance}}}^{E_j}. \quad (6)$$

The stepwise propagation as described by equations (4) and (5) continues until the average proton energy reaches zero. Hence the depth deposition curve is obtained, from which the Bragg peak can be found. This method, even though it uses water as an approximation for the actual material, yields less than 0.3% error even if the whole imaging object is assumed to consist of cortical bone (Wang *et al* 2010). For air, the error is even less, and it is much more accurate for the phantom studied here as well as the actual human body.

3. Results and discussion

3.1. Interpath deviation of the different path estimates from the real path

Figure 1 shows the path estimates for one sample proton along with the corresponding GEANT4 simulated path. It can be seen that the interpath deviation between the path estimates and the real path is larger near the middle of the path than at either end. For this example, the three path estimates can be ranked in the order of MPP, CSP and SLP in terms of their proximity to the real path.

Figure 2 shows the root-mean-square (RMS) distance between the different path estimates and the real path for 10 000 protons, having an incoming energy of 200 MeV, traversing 200 mm of water. SLP performs worst, while CSP and MPP are close to each other with MPP being closest to the real path. This observation is in agreement with what has been previously reported by Li *et al* (2006). The maximum RMS distance between the real path and the SLP is however less or equal to 0.8 mm, less or equal to 0.445 mm for the CSP, and less or equal to 0.42 mm for the MPP, respectively. Depending on the field of view and image pixel number per axis, such a maximum deviation may translate to a lateral path error below 1 mm, or about 1 or 2 pixels. Note that the maximum RMS distance depends on both the incoming energy and the depth of water traversed. Higher incoming energy reduces the deviation as less scatter occurs, while traversing to deeper depths does the opposite (cf figure 5 of Schneider and Pedroni (1994) in comparison to figure 2 of this paper).

Moreover, not every estimated proton path is associated with an error of this magnitude. It is therefore desirable to characterize the performance of various path estimation methods by looking at the cumulative distribution of the interpath deviations from the real path. Figure 3 shows the cumulative distribution of interpath deviations at all depths between the three path estimates and the real path. It can be seen that MPP is the best estimate, closely followed by CSP. Again SLP is performing worse than either of the other two. About 90% of the pixels on MPP and CSP, and 65% of them on SLP, are within 5 mm the real path. Almost all the pixels of MPP and CSP, and nearly 90% of them on SLP, are within 10 mm of the real path. Note that all path estimates perform well in terms of the cumulative distribution of their maximum interpath deviations from the real path (cf figure 4). Again it is seen that CSP performs almost identically to MPP, with nearly 95% of pixels having a maximum deviation from the real path below 10 mm. SLP performs worse than the other two path estimation methods, but still nearly 70% of pixels have a maximum deviation below 10 mm from the real path.

Our findings can be summarized as follows: the CSP estimation method yields a proton path estimate that is very close to one arrived at using MPP estimation, with SLP having the largest interpath deviation from the real proton path. Considering MPP to be the best possible path estimate, the CSP estimation method performs closely to it, yielding a good proton path estimate with little computational overhead, while SLP is a reasonably good approximation having the smallest computational overhead.

3.2. Relative probability of path estimates

The performance of the SLP and CSP path estimates is also evaluated by determining the percentage of pixels that lie within the 1.00, 0.99, 0.98, and 0.97 probability level envelope around the MPP estimated path. For a given set of entrance and exit proton information, MPP, by definition, is the path that has the highest probability. If the CSP and SLP path estimates produce paths whose pixels along those paths have probabilities that are comparable to MPP, they too can be considered as reasonable path estimates. Following this reasoning, the percentages of all pixels along a path resulting from either the SLP or the CSP path estimation method falling within a certain probability level envelope around the MPP are evaluated using the proton path probability map. Figure 5 shows the cumulative

distribution of the percentage of pixels falling within the indicated probability level envelopes around the MPP. From figure 5 we find that almost all of the CSP pixels and 90% of the SLP pixels are within the 99% probability level envelope around the MPP. For both the CSP and SLP path estimation methods, almost all pixels fall within the 97% probability level envelope around the MPP. This implies that paths estimated using the CSP or SLP path estimation method are not much less probable than the MPP path estimation. Therefore, CSP and SLP can be considered as good path estimates since almost all pixels lie within the 97% probability level envelope around MPP, which is by definition the most probable path estimate of the real path.

3.3. Image reconstruction using the path estimates

A 4 mm axial slice of the phantom was reconstructed using each of the three path estimation methods for the same simulated proton data set, which gives a dose of 1.45 mGy to the center of the phantom. For comparison, a pCT image has also been reconstructed using the simulated real path, supposedly having no path error at all. As can be seen from figure 6 the image reconstructed using the real path has the highest spatial resolution; the boundary between different elliptical regions is sharp and clear. There are some artifacts in this image due to the way GEANT4 processes energy loss across the boundary between different geometries. This effect is currently under investigation by our group. Images reconstructed using SLP, CSP and MPP look fairly similar, with the pCT image reconstructed using the SLP estimated path having the lowest spatial resolution. Note that even in the image reconstructed with MPP, the boundaries between different low-contrast ellipses are not clear. This is because MPP, though most probable, is still an estimate, while the exact proton trajectory near a boundary is unknown, leading to a blurred boundary between low-contrast geometries in the reconstructed image.

As stated earlier the visual quality of the reconstructed pCT image, such as spatial resolution, is not critical to the application of pCT for dosimetric verification of proton therapy just prior to daily treatment. What is of importance for dosimetric verification is the quantitative accuracy of the reconstructed stopping powers. The average stopping power and its standard deviation were measured in each elliptical region, and compared to the ground truth. Figures 7(a) and (b) summarize our results. As can be seen from figures 7(a) and (b), the pCT reconstructions using SLP, CSP, MPP and the real path all yield correct average stopping powers ($<0.5\%$ error), and their standard deviations are close to those obtained using the real path. In other words, reconstruction using SLP, CSP, or MPP yields a pCT image with correct stopping powers, even though SLP and CSP are poorer path estimation methods than MPP. Also note that using the real path in pCT reconstruction does not reduce image noise, which is expected since the major source of noise in pCT reconstruction is energy straggling (Schulte *et al* 2005). Hence, the SLP and CSP estimation methods are no worse than MPP in terms of reconstructing the correct stopping power.

3.4. Bragg peak prediction using image reconstructed from path estimates

The ultimate validation of a reconstructed stopping power pCT image is its usefulness to predict the Bragg peak of a known incoming proton beam accurately occurring on it. Figures 8(a) and (b) show two examples of the predicted integral depth dose curve as well as the

Bragg peak. pCT images reconstructed using each of the three path estimation methods as well as the real path at an imaging dose level of 0.09 mGy were employed. Note that the imaging dose is about two orders of magnitude lower than that used for normal x-ray CT. The Bragg peak prediction has been carried out over a range of imaging dose levels and it was found to be feasible for all imaging dose levels tested. An imaging dose of 0.09 mGy is at the lower end of the imaging dose range tested, and has therefore been chosen to illustrate the accuracy of our method. Figure 8(a) shows the depth dose curve for a 90 MeV proton pencil beam entering from the left of the phantom; figure 8(b) shows the depth dose curve for a 120 MeV proton pencil beam entering from bottom of the phantom. In both cases the energy deposited along the proton path as a function of depth is calculated based on the stopping power images using the method as described in section 2.5, and is compared with that obtained from simulation. As can be seen from figures 8(a) and (b), the Bragg peak location is successfully predicted within 1 mm of its actual occurrence on the pCT image reconstructed using the real proton path.

Note that the predicted range of the protons by each of these methods might not agree with the one obtained using GEANT4 simulation, and the energy deposited at every point along the path might differ from the simulated value, which is due to the CSDA assumption, straight-line proton beam assumption, as well as image noise. However, the location for the maximum proton energy deposited in the phantom, i.e. the Bragg peak, can accurately be found using any of the proton path estimation methods, which is of importance for the application of pCT in proton radiation therapy as a dosimetric pre-treatment verification tool for where the Bragg peak in the patient will occur for a given treatment fraction due to changes in internal anatomy. Moreover, a more exact depth dose curve could be obtained employing a more realistic depth dose curve fitting method (like the one by Bortfeld 1997) other than the simplistic one proposed in section 2.5.

Our results show that stopping power reconstruction using SLP or CSP can be employed in pCT image reconstruction for accurate prediction of the Bragg peak in most cases. One situation in which Bragg peak prediction might not succeed occurs when the incoming proton beam is parallel to a heterogeneity boundary and stops on it. Due to the low resolution of pCT near low-contrast geometry boundaries, Bragg peak prediction may not succeed for this scenario. Nevertheless, pCT images are still clinically useful for daily pre-treatment Bragg peak location verification prior to proton treatment in most treatment scenarios.

4. Conclusion

This study has characterized the performance of straight line and cubic spline proton path estimation methods as compared with the most-probable proton path estimation method. Although SLP and CSP yield poorer proton path approximations than the MPP method does, it has been shown that both of them are sufficient to yield an accurate stopping power pCT image that can be used for daily pre-treatment Bragg peak location verification.

Since energy uncertainty dominates the quantitative error of pCT reconstruction (Schulte *et al* 2005), path uncertainty does not play a significant role in the quantitative accuracy of

reconstructed stopping powers, except in regions near geometry boundaries. Although employing SLP or CSP for pCT may yield images of lower spatial resolution, these pCT images nonetheless can be employed for the accurate prediction of the Bragg peak location for a given incoming proton energy. Images reconstructed using SLP or CSP employing an ~0.1 mGy proton imaging dose level can correctly predict the Bragg Peak location within 1 mm accuracy for a 100 mm proton range. Therefore, SLP and CSP may be chosen as path estimation methods for practical pCT reconstruction for dosimetric pre-treatment verification since they are mathematically simpler and hence computationally faster than MPP.

If the straight-line path estimate is used for pCT reconstruction, the hardware design of the pCT detector may be significantly simplified. Because no direction information is needed for the SLP estimation, therefore the pCT detection system when SLP is employed only needs to be able to detect the entrance and exit position and the entrance and exit energy of each proton. However, the applicability of such a simplified pCT design needs to be further validated in future research.

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Figure 1.

An example of SLP, CSP, MPP, and the real path through 95 mm water. This example is chosen for the purpose of clear illustration; most of the proton tracks in the simulation have smaller vertical deflection than the one shown here.

Figure 2.
RMS deviation of SLP, CSP and MPP from the real path as a function of depth for 10 000 simulated protons through 200 mm water.

Figure 3. Cumulative distribution of lateral deviations of SLP, CSP and MPP from the simulated real path.

Figure 4.
Cumulative distribution of the maximum lateral deviations of SLP, CSP and MPP from the simulated real path.

Figure 5.
Percentage of pixels falling within a given probability level envelope around the MPP.

Figure 6. Examples of reconstructed images at 1.45 mGy to the center of phantom using the real path, SLP, CSP, and MPP.

Figure 7.
 (a) Average stopping power and (b) their standard deviation in different ellipse regions of the reconstructed image.

Figure 8.

Bragg peak prediction on the pCT image reconstructed at a dose level of 0.09 mGy. (a) For a 90 MeV proton incoming from left of the phantom. (b) For a 120 MeV proton incoming from the bottom of the phantom.