Technical note

Evaluating the usefulness of the direct density reconstruction algorithm for intensity modulated and passively scattered proton therapy: Validation using an anthropomorphic phantom

Keisuke Yasui a, *, Rie Muramatsu b, Takeshi Kamomae c, Toshiyuki Toshito b, Fumitaka Kawabata c, Naoki Hayashi a

a Fujita Health University, Faculty of Radiological Technology, School of Health Sciences, 1-98 Dengakugakubo Kutsukake-cho, Toyoyaka, Aichi 470-1192, Japan
b Nagoya Proton Therapy Center, Nagoya City University West Medical Center, 1-1-1 Hirate-cho Kita-ku, Nagoya, Aichi 462-8508, Japan
c Nagoya University Hospital, 65 Tsuroma-cho Showa-ku, Nagoya, Aichi 466-8560, Japan

ARTICLE INFO

Keywords:
CT reconstruction algorithm
DirectDensity
Intensity modulated proton therapy
Range verification

ABSTRACT

Purpose: Accurate calculation of the proton beam range inside a patient is an important topic in proton therapy. In recent times, a computed tomography (CT) image reconstruction algorithm was developed for treatment planning to reduce the impact of the variation of the CT number with changes in imaging conditions. In this study, we investigated the usefulness of this new reconstruction algorithm (DirectDensity™: DD) in proton therapy based on its comparison with filtered back projection (FBP).

Methods: We evaluated the effects of variations in the X-ray tube potential and target size on the FBP- and DD-image values and investigated the usefulness of the DD algorithm based on the range variations and dosimetric quantity variations.

Results: For X-ray tube potential variations, the range variation in the case of FBP was up to 12.5 mm (20.8%), whereas that of DD was up to 3.3 mm (5.6%). Meanwhile, for target size variations, the range variation in the case of FBP was up to 2.2 mm (2.5%), whereas that of DD was up to 0.9 mm (1.4%). Moreover, the variations observed in the case of DD were smaller than those of FBP for all dosimetric quantities.

Conclusion: The dose distributions obtained using DD were more robust against variations in the CT imaging conditions (X-ray tube potential and target size) than those obtained using FBP, and the range variations were often less than the dose calculation grid (2 mm). Therefore, the DD algorithm is effective in a robust workflow and reduces uncertainty in range calculations.

Introduction

Accurate calculation of the proton beam range inside a patient is an important topic in proton therapy [1]. The proton beam range inside the body can be calculated by converting the computed tomography (CT) numbers to the stopping power ratio (SPR) or mass densities, depending on the type of dose-calculation algorithm. Additionally, a conversion table is created to convert the CT number to SPR or mass density. Several methods have been proposed to create a CT number to an SPR conversion table, wherein the stochiometric calibration method and poly-binary tissue model have been mainly used [2–5]. Stochiometric calibration methods involve a certain degree of uncertainty, depending on the materials used [6]. The uncertainty related to the conversion of a CT number to an SPR is dealt with in treatment planning by adding a range margin. Range margins are a combination of several factors (e.g., CT number variation, organ motion, and setup variation), and are treated as proximal and distal margins. The magnitude of the range margin depends on the treatment method of the institution, and uncertainties caused by the CT numbers are assigned as 1–3.5% of the beam range [7,8]. CT numbers are attributed to the X-ray tube potential, target size, and the field-of-view (FOV). For highly attenuating materials such as bone and metallic materials, the effect of beam hardening is more pronounced, thus the variation in CT number of changes in the X-ray tube potential is large [9]. To stabilize CT numbers, the CT image for treatment planning was scanned using a fixed X-ray tube potential. However, the flexible use of an X-ray tube potential can improve the
contrast-to-noise ratio, accuracy of the contour, and optimization of the patient dose [10]. For example, low-energy CT images provide an excellent soft-tissue contrast; however, when the patient size is large, high X-ray tube potential imaging may be desirable to obtain a sufficient signal, which also provides reduced metal artifacts [1]. In addition, CT numbers are affected by beam hardening owing to differences in the target size. It is common to use multiple CT numbers in SPR conversion tables depending on the patient size because the variations in CT numbers have a significant impact on the range variation in particle therapy. The complexity of the procedure, such as the use of different conversion tables, may cause human error; therefore, a simple and robust treatment flow is desirable.

In recent times, a CT image reconstruction algorithm was developed for treatment planning to reduce the impact of CT number variations with respect to changes in the imaging conditions, commonly referred to as DirectDensity™(DD). In DD, water and bone are distinguished, and their effective thicknesses are convoluted in the projection space used for reconstruction [11]. Although, in principle, DD is not expected to improve the accuracy of SPR prediction because it is a reconstruction algorithm that uses single-energy CT, the use of DD is expected to reduce the effects of variations in X-ray tube potential and target size. The usefulness of DD in photon beams has been demonstrated in several publications [12-14]. It was inferred from these studies that DD minimizes changes in the dose distribution, improves the robustness of the treatment planning process, and allows for flexible use of the X-ray tube potential. However, to the best of our knowledge, DD has only been studied in proton therapy as a validation of the conversion accuracy of proton therapy treatment planning [15], and the impact of changes in the X-ray tube potential and target size on dose distribution has not been explored. Therefore, we investigated the robustness of DD-based treatment planning with respect to variations in the imaging conditions compared to filtered back projection (FBP). This study will contribute toward improving the proton treatment planning accuracy and workflow robustness. The robustness of DD in proton therapy has not been investigated previously, and the validation of this study provides a reduction in the uncertainty of range estimation.

Materials and methods

The overall schematic flow of this study is shown in Fig. 1. For all imaging conditions, image reconstruction was performed using both FBP and DD, and the results were compared. The examined issues included the impact of the X-ray tube potential and target size variation. A SOMATOM Confidence RT Pro (Siemens Healthcare, Erlangen, Germany) CT scanner was used in this study.

DirectDensity™

As described previously, it is not desirable to use the same X-ray tube potential for all patients. In certain instances, low-energy images are useful to improve soft-tissue contrast; while in other cases, high-energy images are more desirable to improve the signal-to-noise ratio [1,13]. In principle, the DD algorithm holds the potential to apply various X-ray tube potentials in CT for treatment planning because it can reduce the variations in the image values caused due to changes in the imaging conditions. DD utilizes thresholding to distinguish between bones and water or soft-tissues. The effective water thickness of the water and bone is then calculated via the underlying physical attenuation model and synthesized to generate electron and mass density projections. The CT image is generated using a back projection of the electron and mass density projections [11,14,16]. This reconstruction algorithm can produce relative electron and mass density images (DD-image) with an equivalent image value at any energy, without any additional user calibration [15]. In this study, the DD-image value was converted to SPR, and an SPR conversion table was created according to the following procedures.
We used the Electron Density Phantom Model062 (CIRS, Ltd.) to create a CT-image-value-to-SPR conversion table (Fig. 1(a)). For a large target size, we investigated the change in the SPR conversion table when FBP and DD were used by scanning at the X-ray tube potentials of 80 kVp, 120 kVp, and 140 kVp. The X-ray tube potential was fixed at 120 kVp for the small target size, and the effect of the target size was verified by comparing the conversion table with that for the large target size. The FOV was fixed at the extra-large (LL) size (FOV = 500 mm), as done in clinical conditions. In total, four different SPR conversion tables for FBP and DD were obtained and evaluated. Because the anthropomorphic phantom does not contain any metals, the electron density phantom does not include any metals.

In FBP, SPR was calculated using human tissues, as described in ICRU reports 44 and 46, based on the use of the stoichiometric calibration proposed by Schneider et al. [2,17,18] for all CT conditions [2,17,18]. Four different Hounsfield unit (HU) image values were converted using the SPR conversion tables according to the SPR calculated based on each material image. Because the method of converting the DD-image value to the SPR has not yet been established, the DD-image values with respect to the SPR conversion tables were created using the SPR of each material in the electron density phantom directly and obtained by linearly interpolating between each data point of the phantom materials.

**Anthropomorphic phantom planning**

In this study, two types of anthropomorphic phantoms (head and pelvis) were used to emulate clinical conditions. The contour of the treated patient was fused in each phantom. For the head phantom, tumors (clinical target volume: CTV) and organs at risk (OAR: brainstem, eyes, optic nerves) were contoured; for the pelvis phantom, prostate (CTV) and OAR (rectum, bladder, and femoral head) were contoured. We used intensity modulated proton therapy (IMPT) with the worst-case optimization [19] for the head phantom, and the parameters of worst-case optimization were 3 mm in each direction and 3.5% for range uncertainty. The value of 3 mm was fixed based on the setup error and machine variability at the Nagoya Proton Therapy Center. A passively scattered proton beam was used for the pelvis phantom; the range margins were set to 3 mm + 3.5% of the beam range. Treatment plans were created using two or three fields: 90° and 270° opposed fields for the pelvis phantom, and 0°, 90°, and 270° for the head phantom. We use VQA (Ver. 3.0.1 Hitachi, Ltd., Ibaraki, Japan), a treatment planning system commercially available in Japan, which is the first system to use a triple Gaussian kernel model for dose calculation. [20,21]; the dose calculation grid was 2 mm.

Fig. 1(b) shows the validation flow in conjunction with the use of anthropomorphic phantoms. Each anthropomorphic phantom was scanned under the reference conditions (120 kVp, LL-size FOV), and the CT images obtained using the two image reconstruction algorithms were used to create a validation treatment plan. The plan was then copied onto the verification CT image (80 kVp and 140 kVp images) and recalculated to evaluate the range variation. Range variation was evaluated based on the change for a dose depth of 80%. The range verification of the head phantom was analyzed for two fields: 0° and 270°. In addition, the treatment plan for the head phantom was recalculated by changing to an SPR conversion table based on a smaller electron density phantom to verify the effect of target size. The recalculated dose distribution was then performed in the same way to evaluate the change in dosimetric quantities due to the target size variations. Dosimetric quantity variations were evaluated as changes in the maximum dose (D\text{max}) of OARs and the 95% dose (D\text{95\%}) of the CTV.

**Results**

**Variations in SPR conversion table**

The variations in the SPR conversion table with respect to changes in the X-ray tube potential and target size is shown in Fig. 2. As shown in Fig. 2(a), the SPR conversion table varied depending on the imaging conditions in FBP. The effect of the X-ray tube potential change is particularly remarkable for bone-substitute materials. However, DD shows a slight variation with respect to energy change (Fig. 2(b)). FBP employs stoichiometric calibration; therefore, the conversion table of the soft tissue (zoom-in view) is smooth, and the SPR around HU – 100 varies depending on the energy. Meanwhile, the DD-image uses the image value of each material; therefore, irregular image values are seen in soft tissues, although there is a slight variation depending on the imaging conditions.

**Variations in proton range and dose distribution**

Fig. 3 illustrates the variations in the pelvis phantom plan for various X-ray tube potentials. Because of the small amount of bone-substitute materials, the range variations of the X-ray tube potential are minor. In FBP, the range variation observed was -4.0 mm (2.1%) when the X-ray tube potential was changed to 80 kVp, and 1.6 mm (0.8%) when it was changed to 140 kVp. Conversely, in the case of DD, the maximum range variation observed was ±1.9 mm (1.2%) as a result of changes in the X-ray tube potential. The dose-difference image shows the overall range variation. The range variation is particularly noticeable when there are several bone-substitute materials in the beam path. It should be noted that the negative sign indicates under-ranging.

Fig. 4 illustrates the variations in the head phantom plan for various X-ray tube potentials. Compared to the prostate plan, the maximum range was shorter, though the range variation was greater. The shape of the inhomogeneous depth-dose distribution was not affected, and an overall range variation was observed. The range variation due to changes in the X-ray tube potential was considerably large (-12.5 mm; 20.8%) in case of FBP, while the DD algorithm showed a range variation up to ~3.3 mm (5.6%).

The range variation according to the target size is shown in Fig. 5. Similar to the X-ray tube potential variations, the observed range variation was greater in FBP (up to 2.2 mm; 2.5%) and lesser in DD (up to 0.9 mm; 1.4%). Table 1 presents the numerical data. The range variation in case of DD was smaller than that of the dose calculation grid (2 mm), with the exception of one field of the head phantom plan (120 kVp vs. 80 kVp, gantry angle 0°).

**Variations in dosimetric quantities**

Fig. 6 shows the changes in the dosimetric quantities at different target sizes, wherein the variations observed in the case of DD are less than those of FBP for all dosimetric quantities. The variation in the right optical nerve (ONR) (ONR) in case of DD was one-fifth of that of FBP. The dosimetric quantities of the reference scenario are: 44.3 GyE (Brainstem: D\text{max}), 37.5 GyE (Eye left: D\text{max}), 34.4 GyE (Eye right: D\text{max}), 42.6 GyE (Optic nerve left: D\text{max}), 42.9 GyE (Optic nerve right: D\text{max}) and 82.5% (CTV: D\text{95\%}).

**Discussion**

In this study, we verified the usefulness of the DD algorithm in proton therapy. In conclusion, the dose distributions using DD were more robust with respect to variations in the CT imaging conditions (X-ray tube potential and patient size) than those in case of FBP, and the range variations were often less than the calculation grid. The range variations observed in case of DD were smaller than those of FBP; however, in case of DD, a large variation was observed for the head phantom with the...
bone-substitute material.

A notable feature of the DD algorithm is that the results are robust with respect to variations in the target size. In proton therapy, multiple SPR tables are often used to reduce range uncertainties with respect to changes in the beam hardening effect caused by the target size. However, this approach does not accommodate variations in the patient’s size or target size during a series of images. Furthermore, while using multiple SPR tables, it is necessary to select the appropriate table according to the imaging conditions, which should be simplified because of the risk of human error. The results of this study demonstrate that DD can reduce the uncertainty of dose calculation due to differences in patient size and provide a robust workflow. Upon comparing the dosimetric quantities, there was no observable difference between the FBP- and DD-images at 120 kVp. These results are similar to those obtained in previous studies on photon radiation [12]. Conversely, the improvement in robustness with respect to patient size variations is indicated in the DD-image by analyzing the dosimetric quantities, which supports the usefulness of DD in proton therapy.

The DD algorithm also showed excellent results, compared to FBP, in terms of X-ray tube potential variations. Using different X-ray tube potentials has its advantages, including improved contour accuracy and reduced radiation dose. DD has the potential to be applied in low-energy imaging for treatment planning, although further research is required because of the large variations in the range of high-density materials. CT number variations are related to the CT imaging conditions, and appropriate quality control is required for accurate range calculation. Thus, dose distributions using DD-based SPR conversion tables could be robust against range uncertainties.
Currently, a range margin is set for the uncertainty of the beam path in proton therapy planning. In general, a margin used to compensate for the uncertainty of the beam path (1–3.5% of the beam range) is added to the systematic range margin (1–3 mm) \[7,8\]. By using the DD algorithm, it is possible to reduce the margin by considering the beam range. In the case of DD, the variations in the dosimetric quantities with respect to...

---

**Fig. 4.** Validation results using the head phantom at different X-ray tube potentials. Depth-dose variations on the central axis in case of (a) FBP and (f) DD. Dose distribution of three fields with (b) 120 kVp (FBP), (c) 80 kVp (FBP), (g) 120 kVp (DD), and (h) 80 kVp (DD). Dose-difference images with (d) 120 kVp vs. 80 kVp (FBP), (e) 120 kVp vs. 140 kVp (FBP), (i) 120 kVp vs. 80 kVp (DD), and (j) 120 kVp vs. 140 kVp (DD) (G0: gantry 0° beam, G270: gantry 270° beam).

**Fig. 5.** Validation results using the head phantom for target size variation. Depth-dose variation on the central axis in case of (a) FBP and (c) DD. Dose-difference images of three fields calculated using large SPR vs. small SPR tables in the case of (b) FBP and (d) DD (G0: gantry 0° beam, G270: gantry 270° beam).
changes in the target size were observed to be less than half of those observed in the case of FBP. In clinical practice, multifield irradiation is often used. This study was only verified using an anthropomorphic phantom; thus, verification in actual clinical cases is essential.

The limitation of this study is the accuracy of converting the DD-image value to the SPR. Our method directly applies the DD-image value to the SPR. Our method directly applies the DD-image value to the SPR. However, DD is a single-energy CT reconstruction algorithm, and in principle, it is difficult to accurately predict the SPR. The accuracy of creating a conversion table using DD could improve by adding the variability of human tissues [22]. In addition, although we did not include any metals, it is important to note that small metal parts (e.g., small clips) may be included in clinical cases. Although the accuracy of converting the DD-image value to the SPR is not completely satisfactory, and the stoichiometric methods depend on the tissue substitutes used during calibration [6]. Therefore, we believe that the DD algorithm will be one of the most useful processes in the future. In recent years, a method was developed to calculate the stopping power directly using dual-energy CT [23–25]. By using dual-energy CT, the SPR can be estimated based on the actual CT date of patient, which improves the robustness of dose distribution. However, dual-energy CT is expensive and has several hardware limitations. In principle, the DD algorithm can be used with existing CT systems, and it has been shown to be an excellent process to improve the planning workflow and reduce uncertainties relating to CT-image value to the SPR conversion.

Conclusions

The advantages associated with the use of DD (a novel CT reconstruction algorithm) for proton therapy were investigated. DD could be more robust against to target size variations. However, although the range variation for changes in the X-ray tube potential improved, certain range variations still exceeded the calculation grid. The dose distributions using DD-images are robust against variations in the CT imaging conditions, thereby suggesting that the DD algorithm is effective in a robust workflow and reduces uncertainty in range calculations. Although the accuracy of converting the DD-image value to the SPR needs to be verified, DD is a promising algorithm for application in proton therapy.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References


Table 1

The total numerical data for the range variations observed in all investigated cases. The negative sign implies that the range is shorter. Absolute variations (mm) and relative variation (%; 80% dose level) are shown.

<table>
<thead>
<tr>
<th>Absolute variation (Relative variation)</th>
<th>FBP 120 kVp vs. 80 kVp</th>
<th>120 kVp vs. 140 kVp</th>
<th>Large vs. Small</th>
<th>DD 120 kVp vs. 80 kVp</th>
<th>120 kVp vs. 140 kVp</th>
<th>Large vs. Small</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate Field 1</td>
<td>3.7 mm (2.0%)</td>
<td>1.6 mm (0.8%)</td>
<td>–</td>
<td>1.9 mm (1.0%)</td>
<td>1.2 mm (0.6%)</td>
<td>–</td>
</tr>
<tr>
<td>Field 2</td>
<td>4.0 mm (2.1%)</td>
<td>1.6 mm (0.8%)</td>
<td>–</td>
<td>1.9 mm (1.2%)</td>
<td>1.3 mm (0.6%)</td>
<td>–</td>
</tr>
<tr>
<td>Head Field 1</td>
<td>12.5 mm (20.8%)</td>
<td>3.3 mm (5.5%)</td>
<td>–</td>
<td>3.3 mm (5.6%)</td>
<td>1.2 mm (2.2%)</td>
<td>–</td>
</tr>
<tr>
<td>Field 2</td>
<td>7.9 mm (8.7%)</td>
<td>2.0 mm (2.2%)</td>
<td>–</td>
<td>1.3 mm (1.4%)</td>
<td>0.9 mm (0.9%)</td>
<td>–</td>
</tr>
</tbody>
</table>

Fig. 6. Variations in the dosimetric quantities using the head phantom for object size variation (EyeL: Eye left, EyeR: Eye right, ONL: Optic nerve left, ONR: Optic nerve right, CTV: Clinical target volume).


