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FULL PAPER

Automatic contrast medium extraction system using electron density data with dual-energy CT

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Objective: The purpose of the current study is to create a contrast medium extraction method using raw-data-based electron density (rED) and CT number from dual-energy CT (DECT) for automatic delineation of the contrast region.

Methods: A CT-ED phantom containing tissue-equivalent inserts and an acrylic phantom with an iodinated contrast medium were scanned by DECT. The contrast medium extraction system was created using Python. The accuracy of the contrast medium extraction was evaluated by measuring the diameter in terms of the full width at half maximum (FWHM) and the ratio of the volume (ROV).

Results: Mean-2SD CT numbers and the difference of the CT numbers (DCT) of the contrast medium at 0–130 mg ml⁻¹ contrast medium concentration and the bone materials were more than –33 and –20 HU, respectively. In the correlation of rED and CT number, the gradient with the contrast medium phantom was greater than that with the CT-ED phantom. The accuracy of the contrast medium at 80 kV/135 kV and 100 kV/135 kV tube voltages. The gradient of the CT-ED and contrast

medium phantoms were different. The gradient in the CT-ED phantom and the contrast medium was 0.0012 and 0.0003 at 80 kV/135 kV, and 0.0015 and 0.0005 at 100 kV/135 kV tube voltages, respectively. The ratio of the measured to the actual diameter in FWHM and ROV was 0.98–1.00 at 2–130 mg ml⁻¹. At a tube voltage of 100 kV/135 kV. The ratio of the measured to the actual diameter in ROV was 0.66 and FWHM was 0.90 at 2 mg ml⁻¹ contrast medium concentration. The ratio of the measured to the actual diameter in FWHM and ROV was 0.98–1.00 at 3–130 mg ml⁻¹.

Conclusion: We created the contrast medium extraction method with rED and CT number images. The contrast medium extraction method could be used with DECT images at 80 kV/135 kV. The method is expected to only extract images from the region containing the contrast medium.

Advances in knowledge: We created the contrast medium extraction method using raw-data-based electron density and CT number from DECT and it is expected to only extract information from the region containing the contrast medium.

INTRODUCTION

In modern radiotherapy treatment planning, CT is a fundamental and primary method for accurate delineation of surface contours and internal structures, including targeted and critical organs. CT numbers are measured in Hounsfield units (HU) and provide tissue electron density (ED) information, which allows one to perform a pixel-by-pixel correction for tissue inhomogeneity when calculating dose distributions in a single-energy CT (SECT). However, ED does not accurately correlate

to CT number because the CT number depends on the ED and the effective atomic number. Dual-energy CT (DECT) can yield material-specific information using material decomposition algorithms that analyse the change in tissue attenuation between low- and high-energy scans.^{1,2} The DECT can also reduce beam-hardening artifacts and provide more quantitatively accurate attenuation measurements in these images. Although SECT images can only provide CT number information, one can use DECT to obtain various other data, such as the

Figure 1. (a) CT-ED phantom: electron density phantom model 062M, (b) acrylic phantom containing different concentrations of iodinated contrast medium.

effective atomic number and mono-energetic CT number.^{3,4} There are four types of DECT scanners available that differ in the technique used to acquire high- and low-energy CT data-sets. These are the dual-source dual-energy scanner, single-source dual-energy scanner with fast kilovoltage switching, single-source dual-energy scanner with dual detector layers, and single-source CT switching voltages between gantry rotations. The current study used single-source CT switching voltages between gantry rotations. An advantage of this approach is to perform the sinogram-based reconstruction with low and high-kV sinogram images. Other approaches use image-based reconstruction that the electron density image is created from the reconstruction CT images. Thus, raw-data-based electron density (rED) data created by showed little effect on the metal artefact based on the CT image.⁵ There is a possibility that using the rED images would further reduce image artifacts and improve material decomposition accuracy.

In treatment planning, a contrast medium has been used to obtain accurate delineation of targeted volumes and organs at risk. Thus, the use of a contrast medium is necessary in situations where contrast is likely to improve the accuracy of the targeted or normal structure delineations. Usually, a water-soluble contrast agent was used, and this was washed-out after a scanned CT. However, Lipiodol, which was a mixed anti cancer agent and an oily contrast medium, is still used in actual treatment situations. Our previous study reported the dosimetric impact of Lipiodol in liver stereotactic radiation therapy.⁶ The results depended on the material assignment method in the dose calculation. Not all materials have been used in CT-ED correction tables. The material assignment has been performed using a CT-ED correction table that only

considered human tissue equivalent materials. Thus, we must identify the contrast medium and extract the targeted region. Meanwhile, in radiation diagnosis, contrast-enhanced CT has often been performed to enhance the contrast between lesions and tissue. Nicola *et al* reported both anatomic and functional information about the lungs in a variety of pulmonary disease states based on a single contrast-enhanced CT examination. Moreover, the contrast medium is often used for better visualisation of the tissue of interest.⁷ The contrast medium is used to enhance the tumour region. If it is possible to extract the contrast medium enhanced region, only the lesion would be extracted. Thus, contrast medium extraction images are required for radiation therapy and radiation diagnostics. DECT images with commercial software could obtain iodine contrast enhanced images and virtual non-contrast images. However, the contrast-enhanced images could not eliminate the CT numbers in images but enhance the CT numbers in the region of interest. Moreover, DECT could create the iodine maps that showed uptake of iodinated contrast enhanced region. Although the past study reported that the iodine map improved the detection of these lesions in the pancreatic cancer, it could not eliminate the bone region.⁸

In the current study, we investigated the correlation between the rED and CT number, and we created the contrast medium extraction method using rED using sinogram data and CT number from DECT.

METHODS AND MATERIALS

Figure 1 shows the two phantoms used in this study. One was a CT-ED electron density phantom model 062M (Computerized Imaging Reference Systems, Inc., Norfolk, VA) (Figure 1a).

Figure 2. An overview of the contrast medium extraction system.

The other phantom contained several tissue-equivalent inserts, including a lung inhale, lung exhale, adipose, breast, water, muscle, liver, trabecular bone (200 mg cc⁻¹ hydroxyapatite), dense bone (800 mg cc⁻¹ hydroxyapatite), and another dense bone (1250 mg cc⁻¹ hydroxyapatite). The atomic composition and densities were well known and were provided by the manufacturer. Another phantom was made from acrylic (Figure 1b), which included inserts with different concentrations of iodinated contrast medium. Syringes were filled with solutions prepared by diluting the contrast medium (Omnipaque 300, GE Healthcare, Princeton, NY) with water to predetermined concentrations of 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 40, 60, 90, and 130 mg contrast medium per ml. The syringes were positioned around the centre of the phantoms. DECT studies were performed with a 320-detector CT scanner (Toshiba Medical Systems Corporation, Japan). CT scans were performed at tube voltages of 80 kV/135 kV and 100 kV/135 kV as these were the only scan settings that the user could select. Exposures of 800 and 200 mA were used to minimise noise. The time taken to switch the tube voltage between 80 kV and 135 kV was 0.4 s. The remaining scanning parameters were set to 1.0 s rotation time, 0.5 mm slice thickness, and 400 mm field of view.

ED and CT number measurement

The total number of slices was 80, and the midsection of the slices was analysed. ImageJ software package (National Institutes of Health) was used to display the rED and CT numbers. The rED number for each material was calculated by raw-data-based decomposition from the DECT data. In the diagnostic energy range, the linear attenuation coefficient μ of a material can be described using photoelectric absorption and Compton scattering (excluding K -edge effects),

$$\mu(E) = a_p f_p(E) + a_c f_c(E) \quad (1)$$

where E is the photon energy, a_p and a_c are material constants, and f_p and f_c are constants that depend on the E values in photoelectric absorption and Compton scattering, respectively.⁴ This formula can be simplified as

$$\mu(E) = f(\rho_e, Z, E) + f(\rho_e) \quad (2)$$

Figure 3. The reference and the rED values (upper) and deviation between the reference ED and rED values (lower) with the CT-ED phantom.

Figure 4. (a) Measured CT numbers in the CT-ED phantom. (b) DCT values in the CT-ED phantom.

where ρ_e is the rED number and Z is the effective atomic number. In dual-energy processing, a linear attenuation coefficient can be expressed by 2 basis materials as

$$\mu(E) = \mu_1(E) c_1 + \mu_2(E) c_2 \quad (3)$$

where $\mu_1(E)$ and $\mu_2(E)$ are known functions of photon energy. The coefficients c_1 and c_2 are independent of energy and vary spatially. The rED and effective atomic numbers were calculated by solving equations (2) and (3). However, a more detailed parameter required to calculate the rED has not been given to the public. Thus, the accuracy of the rED and CT numbers was investigated first. The mean value and the standard deviation (SD) of the rED and the CT numbers were measured within a manually drawn region of interest (ROI) using ImageJ. The rED measurement accuracy in an electron density phantom model 062M was compared with the reference values. The CT number obtained with 80 kV and 135 kV scans, the CT number correlation at 80 kV, and the rED were analysed in the CT-ED phantom and the acrylic phantom.

The contrast medium extraction method

The contrast medium extraction system was built with Python 2.7. This system is composed of four processes, as shown in Figure 2. The threshold was obtained from the CT numbers (Step 1), from the difference of the CT numbers (DCT) between low-voltage and high-voltage (Step 2), and from the gradient in the rED-CT (Step 3), and the contrast medium concentration was assigned (Step 4). The threshold values were used the mean-2SD CT numbers and DCT values at the 0 mg ml⁻¹ contrast medium concentration in step 1 and step 2. The threshold value of the correlation between the rED and CT number was used the average value of the gradient in the CT-ED phantom and the contrast medium phantom in step 3. After extracting the contrast medium region with these threshold values, the contrast medium concentration was assigned using the correlation between the

Figure 5. (a) Measured CT numbers in the acrylic phantom containing different concentrations of iodinated contrast medium. (b) DCT values in the acrylic phantom containing different concentrations of iodinated contrast medium.

contrast medium concentration and the CT number. 3D median filtering and Gaussian filtering were used to de-noise each image. The accuracy of the contrast medium extraction was evaluated in Step 3 by measuring the diameter in terms of the full width at half maximum (FWHM) between the CT image and the contrast medium extracted image and the ratio of the volume (ROV). ROV was defined by

$$\text{ROV} = \frac{V_{\text{ext}}}{V_{\text{ref}}}$$

where V_{ext} and V_{ref} were defined by the volume which filled the contrast medium. V_{ext} is the volume of the contrast medium extracted using this system and V_{ref} is the reference volume containing the contrast medium. V_{ref} was detected by binarisation from the 135 kV-CT image of the contrast medium phantom. The threshold CT number used in binarisation was 15 HU, which was determined using the CT number in the 135 kV-CT image

Figure 6. (a) rED correlation at 80 kV/135 kV and CT number at 80 kV. (b) rED correlation at 100 kV/135 kV and CT number at 100 kV for CT numbers greater than -33 HU.

of the water material. Binarisation was conducted over the mean ± 3 SD.

RESULTS

Accuracy of the measured rED and the CT number
Figure 3 shows the difference between the rED and the reference electron density provided by the manufacturer of the CT-ED phantom. Without lung inserts, the rED number agreed well within 2.4%. The maximum difference was 4.8% in the lung (inhale) insert at 80 kV/135 kV and 8.6% in the lung (exhale) insert at 100 kV/135 kV. These differences were within SD values.

Measured rED and CT numbers

Figure 4 shows the CT numbers and difference of the CT numbers (DCT) in the CT-ED phantom. Mean-2SD CT numbers from the lung inhale, lung exhale, and adipose were below -33 HU at all tube voltages. On the other hand, mean-2SD CT numbers from the muscle, liver, trabecular bone (200 mg/cc hydroxyapatite), dense bone (800 mg cc⁻¹ hydroxyapatite), and higher density bone (1250 mg cc⁻¹ hydroxyapatite) were greater than -33 HU at all tube voltages. The CT numbers in the high concentration bone materials were larger. The CT numbers of the bone materials were greater at lower tube voltage. Although the mean-2SD DCTs of bone (200 mg cc⁻¹ hydroxyapatite), dense bone (800 mg cc⁻¹ hydroxyapatite), and high density bone (1250 mg cc⁻¹ hydroxyapatite) were greater than -20 HU, while the DCTs of the remaining materials were less than -20 HU. The DCT values from the bone materials at a tube voltage of 80 kV/135 kV were greater than the DCT values gathered at a tube voltage of 100 kV/135 kV.

Figure 5 shows the CT numbers and DCT in the contrast medium phantom, respectively. The CT numbers and DCTs of the contrast medium at all concentrations were obviously greater than HU for all tube voltages. DCT had a high correlation with tube voltage ($r > 0.99$). The DCT of the bone materials gathered at 80 kV/135 kV tube voltage were greater than the DCT gathered at 100 kV/135 kV tube voltage.

Extraction of the contrast medium region

From the result of section B, the mean-2SD CT numbers of the contrast medium at all concentrations was greater than -33 HU, and the DCT was also greater than -20 HU at tube voltages of both 80 kV/135 kV and 100 kV/135 kV. Thus, the threshold values of the CT number and DCT were -33 HU and -20 HU at step 1 and step 2 of the Python program. Next, the contrast medium region was extracted using the threshold of the gradient of rED to CT number at step 3 of the Python program. From the correlation between rED and the CT number, the threshold values were the average value of the gradient in the CT-ED phantom and the contrast medium phantom, which were 0.00075 at 80 kV/135 kV and 0.0010 at 100 kV/135 kV, as shown in Figure 6. The contrast medium concentration was assigned using the correlation between CT number and the contrast medium concentration, as shown in Figure 5 a. From above, the threshold values were assigned in the contrast medium extraction systems, as shown in Figure 7. The iodine density image and the contrast medium extracted images from the CT-ED phantom with contrast

Figure 7. An overview of the contrast medium extraction system (threshold values were included).

Table 1. Limit concentration accuracy of the contrast medium at 80 kV/135 kV

mg ml ⁻¹	1	2	3	4	5	6	7	8	9	10	20	40	60	90	130
ROV	0.00	0.98	1.00	1.00	0.99	0.99	1.00	1.00	0.99	0.99	0.99	0.99	1.00	0.99	0.99
FWHM	0.00	0.98	0.98	1.00	1.00	0.99	1.00	0.99	0.99	0.99	0.98	0.99	1.00	0.98	1.00

FWHM, full width at half maximum; ROV, ratio of the volume.

Table 2. Limit concentration accuracy of the contrast medium at 100 kV/135 kV

mg ml ⁻¹	1	2	3	4	5	6	7	8	9	10	20	40	60	90	130
ROV	0.00	0.66	1.00	0.99	0.99	0.99	1.00	1.00	0.99	0.99	0.99	0.99	1.00	0.99	0.99
FWHM	0.00	0.89	0.98	1.00	1.00	0.99	1.00	0.99	0.99	0.99	0.98	0.99	1.00	0.98	1.00

FWHM, full width at half maximum; ROV, ratio of the volume.

medium concentrations of 2, 4 and 8 mg ml⁻¹ and the acrylic phantom with iodinated contrast medium are shown in Figure 8. Although the contrast medium is highlighted in the iodine-density image, the other materials are not eliminated. Therefore, only the contrast medium cannot be extracted from the iodine-density image. By using the contrast medium extraction system, only the region containing the contrast medium was extracted. The accuracy of the contrast medium at 80 kV/135 kV and 100 kV/135 kV tube voltages is shown in Tables 1 and 2, respectively. The accuracy of the contrast medium limit concentration was 2 mg ml⁻¹ and the ratio of the measurement to the actual diameter in FWHM and the ROV was 0.98–1.00 at 80 kV/135 kV tube voltage. At a tube voltage of 100 kV/135 kV, the accuracy of the contrast medium extraction method was 0.66 for the ROV and 0.90 for FWHM at 2 mg ml⁻¹ contrast medium concentration.

Figure 8. CT image, iodine-density image and the contrast medium extracted images in the CT-ED and acrylic phantoms.

The ratio of the measured to the actual diameter in FWHM and the ROV was 0.98–1.00 at more than 3 mg ml⁻¹ concentration.

DISCUSSION

The rED accuracy was sufficient within 4.8% at 80/135 kV and 8.6% at 100/135 kV for the CIRS 062M phantom. Previous study showed the same trend that the rED accuracy was 5.1% for a Gammex 467 phantom (Gammex, Inc, Middleton, WI).⁹ Thus, rED at 80/135 kV could be reduced the dose difference and it be used for radiation treatment planning without converting the CT number to ED.

CT numbers for bone materials and the contrast medium were higher at lower tube voltage. Thus, DCT at 80 kV/135 kV for bone materials and the contrast medium was also larger than that at 100 kV/135 kV. The photoelectric effect is the predominant interaction with low energy radiation and with high atomic number materials. In the correlation between ED and CT number, it has been considered that the CT number and rED of tissues cannot be interrelated via a simple one-to-one correspondence that is independent of material. This is because the CT numbers estimated from the tissue attenuation coefficients depend on the electron densities and effective atomic numbers. In the previous study, Saito, et al created a method for converting the energy-subtracted CT number to an ED based on this correlation.¹⁰ However, our study revealed that the gradient (>-33 HU) of the CT-ED phantom was greater than that of the contrast medium phantom. From these results, the correlation between CT number and ED was not a one-to-one

correspondence for any materials. The attenuation and the deviation of attenuation due to energy was dependent on the materials. Both the bone materials and the contrast medium showed high CT number and it was difficult to separate them. There is a possibility to separate them using the rED and CT number correlation.

In our study, we developed the contrast medium extraction method. DECT can reconstruct material density images, which provide material-specific information. Two commonly selected DECT basis material pairs are iodine and water. When iodine is paired with water, two separate sets of images (a set of iodine-density images and a set of water-density images) are generated. In the water-density image in an iodine-water image pair generated from the contrast material-enhanced DECT dataset, voxels that show an energy-dependent attenuation change resembling the attenuation of iodine are removed and represented instead on the iodine-density image. The virtual unenhanced images thus generated from the contrast-enhanced dual-energy dataset can provide information equivalent to that from unenhanced images obtained before the administration of contrast material. Although these techniques can reconstruct the enhanced and unenhanced images, it cannot separate the region containing only the contrast medium, as shown in Figure 8. From the result of Figure 8, it was clear that these techniques could not discriminate the contrast medium and bone with slightly different CT numbers. It would be difficult to use the enhanced and unenhanced images for dose calculation in radiation treatment planning because the CT number in the contrast medium and in bone was varied. Our system can fully extract the region containing the contrast medium. Tumours or other diseases that were enhanced by the contrast medium could be extracted using our automatic extraction system.

The ratio of the measured to the actual diameter in FWHM and ROV was 0.98–1.00 at 2–130 mg ml⁻¹ concentration for 80 kV/135 kV and 3–130 mg ml⁻¹ for 100 kV/135 kV. Miyagami, et al reported that the range of the CT numbers in the Lipiodol region in HCC patients were 139 to 3062 HU.¹¹ From the result of the correlation of the CT numbers and the contrast medium concentration in Figure 5, 3000 HU was over 90 mg ml⁻¹ concentration of the contrast medium using over 100 kV. Thus, the contrast medium extraction method is needed to be evaluate at 90 mg ml⁻¹ concentration of the contrast medium. The DCT of the bone materials and contrast medium at 100 kV/135 kV was smaller than at 80 kV/135 kV. At least 98% extraction accuracy of the contrast medium would be acceptable if the rED accuracy uncertainties are within

5%. In the previous study, Izmirli et al investigated that the effect of calculated dose at various contrast medium concentrations in treatment planning systems for different dose calculation algorithms.¹² Izmirli et al reported that the dose difference for treatment plans with and without the contrast medium was within 2.2% at less than 2 mg ml⁻¹ concentration. The contrast medium extraction method could be useful by using DECT images at 80 kV/135 kV for radiation treatment planning. Moreover, automatic extraction of the contrast-enhanced tumour or other diseases would be useful in radiation treatment planning and radiation diagnosis. Inter observer variability in target volume delineation is a serious problem in successful radiation treatment planning and radiation diagnosis.^{13,14} Fujigai et al reported hepatocellular carcinoma enhancement of more than 100 HU in the hepatic arterial phase and portal venous phase. Moreover, Zhu et al found that a pulmonary artery (PA) enhancement of 431 HU is used on average for pulmonary embolism diagnosis.¹⁵ From the correlation of the iodinated contrast medium concentration, the CT numbers were 40–75 HU at 2 mg ml⁻¹ concentration. Thus, these tumour or diseases could be extracted by using the contrast medium extraction method of DECT images at 80 kV/135 kV. The limitation of this study was that we do not use clinical images. The limitation of the current study was that it was performed the phantom study. There is significant time delay between the high and low energy scans using the single-source CT switching CT used in the current study, this method is subject to artifacts and misalignments due to biological motion or bulk patient motion. Further study regarding that the extraction accuracy and the effect of dose calculation in real patients should be performed.

CONCLUSION

We created a contrast medium extraction method using rED and CT numbers from contrast images. The contrast medium extraction method could be useful at more than 2 mg ml⁻¹ contrast medium concentration by using DECT images at 80 kV/135 kV. The method is expected to extract only the region containing the contrast medium from a patient CT image. Further experiments would be required that the effect of the dose calculation on radiation therapy and lesion detectability on radiation diagnosis using the clinical patient CT image.

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