Diagnostic Performance of Dual-Layer Computed Tomography for Deep Vein Thrombosis in Indirect Computed Tomography Venography

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**Background:** The aim of this study was to evaluate the quality and diagnostic performance of virtual monochromatic images (VMI) obtained with dual-layer dual-energy computed tomography (DL-DECT) during indirect CT venography (CTV) for deep vein thrombosis (DVT).

**Methods and Results:** This retrospective study was approved by the Institutional Review Board, which waived the requirement for informed consent. We retrospectively enrolled 45 patients who underwent CTV with DL-DECT, and VMI were retrospectively generated. We compared the venous attenuation, noise, contrast, and contrast-to-noise ratio (CNR) between VMI with the highest CNR and conventional CT on paired t-test. Furthermore, we compared the pooled area under the curve (AUC) of each technique with Delong’s test in 34 patients who underwent color Doppler ultrasonography. The 40-keV VMI had the best CNR. The noise was significantly lower on 40-keV (9.7±2.5 HU) than on 120-kVp VMI (10.5±2.5 HU; P<0.01). The contrast (120-kVp, 38.2±15.3 HU vs. 40 keV, 131.6±43.6 HU) and CNR (120-kVp, 3.8±1.7 vs. 40 keV, 14.4±6.1) were significantly higher in 40-keV VMI than in 120-kVp VMI (P<0.01). Furthermore, the pooled AUC was significantly higher for 40-keV (0.84) than for 120-kVp VMI (0.78; P=0.03).

**Conclusions:** In indirect CTV, 40-keV VMI obtained with DL-DECT offers better image quality and diagnostic performance for DVT than conventional CT.

**Key Words:** Phlebography; Spiral computed tomography; Venous thrombosis; Virtual monochromatic image; X-ray energy

Pulmonary embolism (PE) is a serious, potentially life-threatening disease that is most often caused by deep vein thrombosis (DVT). Early diagnosis of DVT is important for prevention of PE. A phantom study suggested the usefulness of dual-energy computed tomography (DECT) for decreasing image noise and improving conspicuity and diagnostic accuracy of DVT. Optimal venous enhancement, however, is crucial for the detection of DVT. To increase venous enhancement, either a large volume of contrast medium or a higher concentration of iodine, or low-tube voltage combined with CT venography (CTV), have been used. Venous attenuation ≥80 HU can provide adequate differentiation between the veins and a clot.

DECT can generate virtual monochromatic images (VMI) at different monochromatic X-ray energies (keV) based on 2 different energy datasets. The advantages of VMI include reduced beam-hardening artifacts and more accurate quantitative attenuation measurements. VMI at low keV can increase both contrast enhancement and venous attenuation compared with conventional images, but they also markedly increase image noise. So far, there have been no reports on the usefulness of VMI at low keV for the detection of DVT.

Recently, dual-layer DECT (DL-DECT) has become available for clinical use. DL-DECT can overcome the disadvantage of increased image noise at low energy levels. In a previous study of dynamic hepatic CT, VMI obtained with DL-DECT at lower energy levels had increased image quality and conspicuity of arterial enhancement in hepatocellular carcinoma compared with a conventional 120-kVp protocol, despite a 50% iodine load reduction. To our knowledge, however, no previous study has compared VMI obtained with DL-DECT with the images obtained with a conventional 120-kVp protocol in CTV.

The purpose of this study was to evaluate the image quality and diagnostic performance of VMI obtained with...
Usefulness of Dual-Layer CT for CTV

Methods

Ethics
This retrospective study received institutional review board approval (no. 1367). Informed consent to participate was waived. The duration of this study was from 2016 to 2017.

Patients
Between December 2016 and April 2017, we identified 60 patients who underwent CT with DL-DECT (IQon Spectral CT; Philips Healthcare, Best, The Netherlands) for suspected DVT or PE based on elevated D-dimer or clinical symptoms. Eleven patients were excluded because the scanning was carried out with reduced contrast material dose protocols for severe renal dysfunction (estimated glomerular filtration rate <30 mL/min/1.73 m²) or they underwent CT pulmonary angiography (CTPA) alone. Four patients were excluded because they underwent unenhanced CT for history of allergic reaction to iodinated contrast media or poor general condition. Finally, we analyzed the remaining 45 patients who underwent CTV and CTPA using DL-DECT with the standard dose contrast material protocol in this study. They consisted of 21 men and 24 women (mean age, 68.2 years; range, 34–90 years) with body weight ranging from 32 to 72 kg (mean, 55.3 kg).

CT and Contrast Infusion Protocols
All patients underwent CTV and CTPA with DL-DECT. CTV was acquired in the caudocranial direction from just above the diaphragm to the end of the feet. The parameters for CTV were as follows: peak voltage, 120 kVp; detector collimation, 64×0.625 mm; tube rotation time, 500 ms; and helical pitch (beam pitch), 0.703. Tube current was determined using automodulation (dose right index 24, 162 mAs for the average adult). CTPA was acquired in the caudocranial direction during a single inspiratory breath-hold. The parameters for CTPA were as follows: detector collimation, 64×0.625 mm; tube rotation time, 500 ms; and helical pitch (beam pitch), 1.015.

In all examinations, the contrast medium (600 mgI/kg body weight of iopamidol [Iopamiron-370 or Iopamiron-300; Bayer Yakuhin, Osaka, Japan] or iohexol [Omnipaque-350...
We also performed qualitative image analysis of the 40-keV VMI and conventional CT. First, we set the window setting (window level, 50 HU; window width, 400 HU) on a PACS viewer (Synapse; Fujifilm Medical). Second, 2 board-certified radiologists with 8 years and 21 years of experience with CTV and CTPA used a 4-point subjective scale to independently score the image noise, image contrast, image sharpness, streak artifacts, and overall image quality of CTV at the level of the center of the femur. Both the 40-keV VMI and conventional CT were scored. The 2 readers were blinded to the reconstruction technique and evaluated the randomized CT dataset.

To assess image contrast, the readers evaluated venous contrast enhancement at the lower thigh. The scores for image contrast and overall image quality were 1, unacceptable; 2, acceptable; 3, good; and 4, excellent. Image noise and streak artifacts were scored as grade 1, poor/not evaluable due to severe artifacts impairing accurate evaluation; grade 2, evaluable with moderate artifacts, acceptable for routine clinical diagnosis; grade 3, good with minor artifacts, good diagnostic quality; and grade 4, excellent, no artifacts, unrestricted evaluation. Image sharpness was scored by evaluating venous wall sharpness as grade 1, blurry; grade 2, poorer than average; grade 3, better than average; and grade 4, sharpest. Interobserver disagreement was resolved by consensus. Also, interobserver agreement analysis was performed.

Receiver Operating Characteristics (ROC) Analysis
The diagnostic performance of VMI with the highest CNR and that of conventional CT for DVT was compared using ROC analysis. Of the 45 study patients, 34 underwent color Doppler ultrasonography: 18 patients were diagnosed with DVT and 16 were classified as not having DVT. We used these results as a reference.

One of the authors randomized the order of 68 datasets (i.e., the VMI with the highest CNR and the conventional CT for the DVT group and the control group) and 9 board-certified radiologists reviewed all 68 datasets on a PACS viewer (View R version 1.24.05; Yokogawa Electronic, or Omnipaque-300; GE Healthcare, Princeton, NJ, USA) was delivered by a power injector (Dual Shot GX; Nemoto-Kyorindo, Tokyo, Japan) >30 s through a 20-G catheter inserted into an antecubital vein. Next, 30 mL saline solution were delivered at the same injection rate. CTV and CTPA began 300 s and 30 s after contrast injection, respectively.\(^{12,13}\)

CT Image Reconstruction
The spectral-based image data were post-processed at a workstation (Spectral Diagnostic Suite; Philips Healthcare) to generate VMI at 17 different energy levels (40–200 keV) with a spectral level of 3 (as per the vendor’s recommendation). DL-DECT uses a model-based iterative reconstruction (IR) algorithm with 7 de-noising levels. Higher de-noising yields more noise reduction. We used conventional CT reconstructed with IR (iDose level 3; Philips Healthcare) as a control. The CTV and CTPA slice thickness was 3 mm and 5 mm, respectively.

Quantitative Image Analysis
A radiologist with 21 years of experience with CTV and CTPA performed quantitative image analysis of axial images. The reader compared venous attenuation (region of interest [ROI] vein) at the level of the center of the femur in 17 VMI and on conventional CT. We selected an ROI of 25 mm\(^2\) in the vein. The ROI size fitted within the vein, excluding the vessel wall and perivascular fat. The mean attenuation and standard deviation (SD) of the great adductor muscle was determined using an ROI of approximately 400 mm\(^2\). The image noise was defined as the SD of the attenuation of the muscle. The contrast-to-noise ratio (CNR) was calculated using the following formula:

\[
\text{CNR} = \frac{\text{ROI}_{\text{vein}} - \text{ROI}_{\text{muscle}}}{\text{image noise}}
\]

We defined the optimized energy level as that resulting in the highest CNR (i.e., VMI at 40 keV).

We compared the venous attenuation, image noise, contrast, and CNR between the 40-keV VMI and the conventional CT.

Qualitative Image Analysis
We also performed qualitative image analysis of the 40-keV VMI and conventional CT. First, we set the window setting (window level, 50 HU; window width, 400 HU) on a PACS viewer (Synapse; Fujifilm Medical). Second, 2 board-certified radiologists with 8 years and 21 years of experience with CTV and CTPA used a 4-point subjective scale to independently score the image noise, image contrast, image sharpness, streak artifacts, and overall image quality of CTV at the level of the center of the femur. Both the 40-keV VMI and conventional CT were scored. The 2 readers were blinded to the reconstruction technique and evaluated the randomized CT dataset.

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**Usefulness of Dual-Layer CT for CTV**

Tokyo, Japan). The readers were blinded to the acquisition parameters, clinical symptoms, color Doppler ultrasonography, and patient age, sex, and clinical follow-up. The readers indicated their confidence level regarding the presence or absence of DVT by placing a mark on a continuous rating scale. The reading time was not limited.

**Statistical Analysis**

We performed statistical analysis with R (version 2.6.1) and Python (version 3.6.3). Kolmogorov–Smirnov test was used to determine the normality of data distribution. All numerical values are expressed as mean±SD. The paired t-test was used in quantitative image analysis to compare 40-keV VMI and conventional CT. We selected the 40-keV VMI because they had the highest CNR. In qualitative image analysis, we compared all qualitative scores between the 40-keV VMI and conventional CT using the Wilcoxon signed-rank test. We used the following interpretation of the kappa coefficients: <0.20, slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, good; and 0.81–1.00, excellent. We calculated the area under the curve (AUC) of 9 readers and the pooled AUC to detect DVT in both 40-keV VMI and conventional CT. We compared the AUC of each protocol using Delong’s test. P<0.05 was considered statistically significant.

**Results**

**Quantitative Image Analysis**

*Figure 1* shows the results of quantitative image analysis. The VMI noise increased as the energy level decreased, but the noise of VMI at all energy levels was significantly lower than that of conventional CT. The venous and muscle attenuation of VMI increased as the energy level decreased. Similarly, the CNR and contrast of VMI increased as the energy level decreased. The CNR of the 40-keV VMI was the highest of all VMI at all energy levels, and we defined 40 keV as the optimal VMI energy level (*Figure 2*). The contrast and CNR at 40 keV were significantly higher than those of conventional CT (P<0.01; *Table 1*). The VMI noise at 40 keV was significantly lower than that of conventional CT.

| Table 1. Quantitative Image Analysis |
|-------------------------------------|
| **40-keV VMI** | **120-kVp CT** | **P-value** |
| Venous attenuation (HU) | 151.6±75.3 | 78.7±23.3 | <0.01 |
| Image noise (HU) | 9.7±2.5 | 10.5±2.5 | <0.01 |
| Contrast (HU) | 131.6±43.6 | 38.2±15.3 | <0.01 |
| CNR | 14.4±6.1 | 3.8±1.7 | <0.01 |

Data given as mean±SD. CNR, contrast-to-noise ratio; CT, computed tomography; VMI, virtual monochromatic image.

| Table 2. Qualitative Image Analysis |
|-------------------------------------|
| **40-keV VMI** | **120-kVp CT** | **P-value** |
| Image noise | 3.8±0.4 | 3.3±0.8 | <0.01 |
| Image contrast | 4.0±0.3 | 2.4±0.7 | <0.01 |
| Image sharpness | 3.9±0.3 | 3.4±0.8 | <0.01 |
| Artifact | 3.7±0.5 | 3.5±0.7 | 0.07 |
| Overall image quality | 3.9±0.3 | 2.8±0.7 | <0.01 |

Data given as mean±SD. All parameters were measured on a 4-point scale, with 1 indicating the lowest quality and 4 indicating the highest. CT, computed tomography; VMI, virtual monochromatic image.

**Qualitative Image Analysis**

*Table 2* lists the results of qualitative image analysis. The values assigned to image noise, image contrast, image sharpness, and overall image quality were significantly higher for the 40-keV VMI than for the conventional CT (P<0.01 for all). There was no significant difference in artifact scores between the 40-keV VMI and conventional CT (P=0.07).

Interobserver agreement regarding image noise, image contrast, image sharpness, artifacts, and overall image quality was rated as fair to good (kappa, 0.47, 0.48, 0.42, 0.51, and 0.63, respectively).

*Figure 3.* Pooled area under the curve to detect deep vein thrombosis on 40-keV virtual monochromatic images vs. 120-kVp conventional computed tomography, by 9 board-certified radiologists.
With DL-DECT, we can retrospectively create a VMI from various energy levels. Generally, venous enhancement is affected by several factors, including patient age, cardiac output, volume of contrast agent, and body weight. Therefore, acquisition of images with optimal venous enhancement is unpredictable, unlike optimal arterial enhancement. Unfortunately, suboptimal images are sometimes acquired, preventing accurate diagnosis of DVT. However, retrospective spectral analysis with adjustment of the optimal X-ray energy can improve poor image quality to diagnosable image quality in most cases.

In this study, the VMI noise at all energy levels was significantly lower than that of conventional CT. The DL-DECT system simultaneously collects low- and high-energy data in the 2 detector layers, at the exact same anatomic location. Therefore, the VMI reconstruction technique can suppress the beam-hardening artifact and anti-correlated noise in photoelectric and Compton scatter images. In this qualitative study, the artifact score at 40keV was lower in VMI than in conventional CT, but this difference was not statistically significant. Model-based IR techniques equipped with DL-DECT can achieve further noise reduction.

In the present study, the IR technique decreased the image noise of VMI compared with conventional CT. Another advantage of DL-DECT is that scans can be performed at the exact same spatial and angular location.

ROC Analysis

Figure 3 shows the pooled free-response ROC curves for the detection of DVT. AUC for the 9 readers are listed in Table 3. The pooled AUC was significantly higher in 40-keV VMI (0.84; 95% CI: 0.79–0.89) than in 120-kVp VMI (0.78; 95% CI: 0.73–0.83; P=0.03). Representative cases are shown in Figure 4.

### Discussion

In our quantitative image analysis, the 40-keV VMI noise was significantly lower than that of conventional CT. Venous attenuation, contrast, and CNR of 40-keV VMI were significantly higher than those of conventional CT. On qualitative image analysis, image noise, image contrast, image sharpness, and overall image quality of the 40-keV VMI were significantly higher than for the conventional CT. There was no significant difference in artifact scores between 40-keV VMI and conventional CT.

VMI obtained with DL-DECT at lower energy levels have been shown to have increased contrast enhancement. In CTV, lower energy levels also resulted in greater contrast enhancement of VMI. Similarly, low-tube-voltage CT improves image quality compared with the conventional 120-kVp protocol.

With DL-DECT, we can retrospectively create a VMI from various energy levels. Generally, venous enhancement is affected by several factors, including patient age, cardiac output, volume of contrast agent, and body weight. Therefore, acquisition of images with optimal venous enhancement is unpredictable, unlike optimal arterial enhancement. Unfortunately, suboptimal images are sometimes acquired, preventing accurate diagnosis of DVT. However, retrospective spectral analysis with adjustment of the optimal X-ray energy can improve poor image quality to diagnosable image quality in most cases.

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Previous rapid-switching DECT and dual-source DECT resulted in misregistration between the high- and low-energy data sets because previous DECT settings did not allow simultaneous scans. DL-DECT overcomes this disadvantage.

Our secondary finding was the clinically acceptable reconstruction time in DL-DECT, which was of the order of minutes. PE is an acute life-threatening condition that requires accurate and rapid diagnostic imaging. Therefore, a clinically acceptable reconstruction time is important. In addition, accurate diagnosis with CTV requires optimal venous enhancement; therefore, retrospective optimization of the contrast with adjustment of the X-ray energy is a reasonable method.

The present study did not identify the optimal method of X-ray imaging. In quantitative image analysis, VMI at 40 keV had a higher CNR than VMI at other energy levels and than conventional CT. The noise at 40 keV, however, was higher than that of VMI at other energy levels.

On evaluation by 9 readers using ROC analysis, VMI at 40 keV with DL-DECT offered better diagnostic performance for DVT than conventional CT in indirect CTV.

**Study Limitations**

This study had some limitations. First, the number of subjects was small, and hence the results might not be generalizable. Second, we did not perform quantitative image analysis of lower-thigh images because limited vascular dilation prevented exclusion of perivascular fat and muscle from the ROI. Third, the interobserver agreement of qualitative image analysis was fair to good. We hypothesize that this discrepancy reflected pristine variances in image quality perception due to differences in experience between the 2 attending radiologists involved in CT readouts. Fourth, we compared only 40 keV defined as the optimized energy level and conventional images for diagnostic performance. The diagnostic performance of other VMI was unknown. Fifth, given that mean volume CT dose index (CTDIvol) was 17.8±8.4 mGy, DL-DECT may have a disadvantage as compared with conventional CT and low-tube-voltage CT with reduced radiation dose. In the previous report, the CTDIvol of CT under an 80-kVp and 120-kVp protocol were 10.3 mGy and 14.9 mGy (contrast media dose, 540 mgI/kg and 690 mgI/kg) on a 64-detector CT. The lower limbs radiosensitivity is low (conversion factor of 0.0060 for male and 0.0073 for female), therefore this radiation dose is not considered to be a severe problem given that the effective dose in this study was 9.6±4.9 mSv.

**Conclusions**

In conclusion, in indirect CTV, 40-kV VMI obtained with DL-DECT offer better image quality and diagnostic performance for DVT than conventional CT.

**Disclosures**

The authors declare no conflicts of interest.

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