A cute pulmonary thromboembolism (PTE) is one of the most common causes of cardiovascular death. According to prospective cohort studies, the fatality rate due to acute PTE ranges from 7% to 11%. Early diagnosis is essential because immediate anticoagulation therapy is highly effective. More than 90% of PTE arises from deep vein thrombosis (DVT) in the lower extremities and approximately one-third of DVT do not produce any symptoms or signs. Therefore, the detection of DVT using non-invasive diagnostic imaging techniques is important for preventing PTE.

Due to advances in multidetector computed tomography (MDCT), pulmonary CT angiography (CTA) has been established as the first-line imaging procedure for patients with suspected PTE. In combination, CT venography (CTV) and pulmonary CTA are diagnostically valuable for the detection of PTE and the identification of embolism in deep abdominal veins and of DVT in the pelvis and legs.

By combining CTV with CTA, the sensitivity for PTE has been increased from 83% to 90% compared to CTA alone. This led to the suggestion that CTA be performed together with CTV in patients with a high probability of PTE based on clinical assessment.

Exposure to increased levels of irradiation and larger amounts of contrast material is an important limitation of CTV. Low-tube-voltage CTV yields better contrast enhancement and allows for a reduction in the radiation dose by 30% and the CM dose by 20% without image quality degradation. The 80-kV CTV with HIR allows for a reduction in the radiation dose by 30% and the CM dose by 20% without image quality degradation.

Key Words: Computed tomography venography; Contrast material; Iterative reconstruction; Low tube voltage; Radiation dose
voltage scanning, however, is increased image noise. An iterative reconstruction algorithm for CT was introduced to help reduce the quantum noise associated with standard convolution-filtered back-projection (FBP) reconstruction algorithms. Although a prior-generation iterative reconstruction algorithm raised image quality problems such as texture changes due to noise reduction, resulting in a “plastic” or “artificial” appearance, a new type of hybrid iterative reconstruction (HIR) algorithm uses 2 complex noise-reduction components, projection and image spaces, to facilitate the use of a higher percentage of iterative reconstruction while maintaining clinically acceptable images. We hypothesized that a combined low-kV and HIR technique can reduce the contrast material dose as well as radiation exposure at CTV of the lower extremities.

The purpose of the current study was to evaluate whether low-kV CTV with HIR can provide sufficient image quality at a reduced radiation and contrast material dose.

Methods

This prospective study received institutional review board approval; prior informed consent was obtained from all patients.

Subjects

The subjects consisted of 40 consecutive patients (26 women, 14 men; mean age, 59.2±18.3 years; range, 17–85 years) undergoing combined pulmonary CTA and CTV between February and March 2011. All had suspected or confirmed PTE and/or DVT. The exclusion criteria were an contraindication for CT (ie, known allergy to iodine contrast material or risk for an allergic reaction), impaired renal function (serum creatinine >1.3 mg/dl), and pregnancy. We randomly assigned the 40 patients to 2 CTV protocols: 20 each were examined at low tube voltage (80 kV) using a reduced contrast material dose (protocol A) or at standard tube voltage (120 kV) using our standard contrast material dose (protocol B).

CT Scanning and Contrast Material Infusion Protocols

All patients underwent CTV after pulmonary CTA on a 64-detector CT scanner (Brilliance-64; Philips Healthcare, Cleveland, OH, USA). Pulmonary CTA was carried obtained in the caudocranial direction during a single inspiratory breathhold. The parameters for pulmonary CTA were: 80 kV, detector collimation 64×0.625 mm, 500 ms tube rotation time, 0.39 helical pitch (beam pitch), and 600 mAs tube current-time product. The parameters for CTV were: 80 kV, detector collimation 64×0.625 mm, 750 ms tube rotation time, 0.61 helical pitch (beam pitch), and 550 mAs tube current-time product (protocol A) and 120 kV and 230 mAs tube current-time product (protocol B). The CTV dose index volume (CTDIvol) was 10.3 mGy and 14.9 mGy for protocols A and B, respectively. CTV under both protocols was performed from just above the diaphragm to the end of the feet in a caudocranial direction. Under protocol A we delivered a reduced contrast material dose of 540 mgI/kg; under protocol B the dose was 690 mgI/kg, our standard dose. In both protocols, iopamidol with an iodine concentration of 300 or 370 mgI/ml (Iopamiron-300 or -370; Bayer Schering Pharma, Osaka, Japan) was delivered at a fixed injection duration of 40 s via a 20-G catheter inserted into an antecubital vein using a double-head power injector (Autoenhance A-250; Nemoto Kyorindo, Tokyo, Japan); this was followed by 40 ml of saline solution delivered at the same injection rate. All patients underwent pulmonary CTA 30 s after the inception of contrast material injection. CTV was started 3 min after the start of contrast material injection.

CT Image Reconstruction

Image reconstruction was in a 35–45-cm display field of view (FOV) depending on the patient’s physique. The reconstruction section thickness and the section interval at pulmonary CTA were 2.5 mm. All pulmonary CTA images were reconstructed with FBP algorithms. The reconstruction section thickness and the section interval at CTV were 3.0 mm. CTV images acquired with protocol A were reconstructed with the FBP and the HIR algorithms (iDose4, Philips Healthcare); under protocol B they were reconstructed with the FBP algorithm. The HIR algorithm allows the user to adjust the image noise level by inputting a parameter called “iDose level” in percentages; the higher the percentage of iDose level, the higher the noise reduction. Based on preliminary studies we applied an HIR level of 60% (iDose level 5) to image reconstruction; it corresponded with a noise reduction factor of 0.63.

Evaluation of the CT Radiation Dose

We calculated the dose length product (DLP) of CTV on the basis of the CTDIvol and the data acquisition length for each patient. We compared DLP rather than the effective dose because the standardized conversion factor from DLP to the effective dose in the lower extremities was 0.0004 mSv/mGy cm at an X-ray tube voltage of 120 kV; it was not provided for an X-ray tube voltage of 80 kV.

Quantitative Image Analysis

All images were reviewed and interpreted on PACS workstations (View R version 1.09.15; Yokogawa Electronic, Tokyo, Japan). Two board-certified radiologists who were blinded to the protocols performed quantitative image analysis on reconstructed 3-mm-thick transverse images. They measured, first, mean venous CT attenuation, calculated at 4 scan levels (the suprarenal inferior vena cava, and the right iliac, right femoral, and the deep vein in the right lower thigh; slice levels 1–4, respectively). If the right deep vein was occluded, we obtained measurements in the left deep vein. Second, they measured contrast enhancement of the vein, defined as the difference between the mean attenuation in the venous lumen and the muscle at the same slice level. The muscles were the greater psoas, the iliac, the great adductor, and the soleus muscle. Third, they measured the image noise, determined as the average of the SD of the attenuation in the venous lumen and the muscle at the same slice level. The muscles were the greater psoas, the iliac, the great adductor, and the soleus muscle.

Table 1. Patient Demographics

<table>
<thead>
<tr>
<th>Sex (M/F)</th>
<th>Protocol A (n=20)</th>
<th>Protocol B (n=20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.8±17.6</td>
<td>60.7±19.3</td>
<td>0.62</td>
</tr>
<tr>
<td>Body height (cm)</td>
<td>158.5±9.9</td>
<td>155.8±10.9</td>
<td>0.42</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>63.8±10.1</td>
<td>59.2±13.9</td>
<td>0.23</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.4±3.5</td>
<td>24.2±4.1</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Data given as mean±SD.
Figure 1. Comparative quantitative image quality analysis obtained in step 1 (protocol A with filtered back projection [FBP] vs. protocol B with FBP). (A) Mean computed tomography (CT) attenuation of the vein was significantly greater under protocol A at all slice levels. (B) Image noise was significantly higher with protocol A at all slice levels. (C) There was no statistically significant difference in contrast-to-noise ratio at all slice levels. *P<0.05.
Figure 2. Comparative quantitative image quality analysis obtained in step 2 (protocol A with hybrid iterative reconstruction [HIR] vs. protocol B with filtered back projection [FBP]). (A) Mean computed tomography (CT) attenuation of the vein was significantly greater under protocol A at all slice levels. (B) Image noise was significantly lower under protocol A at all slice levels except at the level of the iliac vein. (C) Contrast-to-noise ratio was significantly higher under protocol A at all slice levels. *P<0.05.
protocol A reconstructed with HIR and protocol B reconstructed with FBP. We also measured CT attenuation of the central and lobar pulmonary arteries on pulmonary CT angiograms on the original 2.5-mm transverse images. Nine central vessels (the main and left and right pulmonary arteries, 5 lobar arteries, and the lingular artery) were measured separately, and the mean of these was used for further calculations.

**Qualitative Image Analysis**

Images acquired under each protocol were intermixed; available images included reconstructed 3-mm-thick transverse images. Two board-certified radiologists with 8 and 11 years of experience in indirect CTV interpretation and blinded to the protocols independently evaluated the images for graininess, streak artifact, vessel enhancement, depiction of abdominal organs, and overall image quality using a 4-point scale in which 4=excellent, 3=adequate, 2=of limited diagnostic value, and 1=uninterpretable. Pulmonary arterial enhancement was also rated. When the 2 observers disagreed, final determinations were made by consensus. Adjustment of the window level and width was allowed during qualitative assessments. We compared the scores of the 2 protocols.

**Statistical Analysis**

To determine the appropriate sample size for statistical analysis, before this study we performed power analysis using preliminary measurements of the CNR at slice level 2 obtained in 8 additional subjects not included in the final subject group. The difference in the mean CNR and SD of the 2 protocols was 1.9 and 0.2. The parameters for the power analysis were: effect size d=1.38, α=0.05, power=0.95. Based on these results at least 36 subjects were required for a meaningful statistical analysis. All data are expressed as mean±SD. For images obtained under each protocol we compared the patient characteristics, the DLP, and all qualitative and quantitative image parameters. Differences in the means of the 2 protocols containing normally and non-normally distributed data were determined using 2-tailed independent t-test and the Mann-Whitney U-test, respectively. The degree of agreement between the 2 observers at visual evaluation of the images was measured with the κ statistic, and scored as 0, no agreement; >0 and <0.20, poor agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–0.99, almost perfect agreement. P<0.05 was considered to indicate statistically significant difference. We used software for power analysis (G-Power version 3.1.2 available at http://wwwpsycho.uni-duesseldorf.de/abteilungen/aap/gppower3) and for statistical analyses (SPSS version 15.0, SPSS).

### Results

Patient characteristics are summarized in Table 1. There was no significant difference in the age (P=0.62), gender distribution (P=0.52), body length (P=0.42), body weight (P=0.23), or body mass index (P=0.31) between the 2 protocol groups.

#### CT Radiation Dose

The mean DLP of CTV was 1,163.3±73.6 mGy·cm (range, 1,023.3–1,325.5 mGy·cm) under protocol A and 1,616.2±131.9 mGy·cm (range, 1,362.2–1,920.9 mGy·cm) under protocol B. Protocol A resulted in a significant reduction in DLP, corresponding to a radiation dose reduction of approximately 30%.

#### Quantitative Assessment of Image Quality

In step 1, mean venous CT attenuation was significantly greater under protocol A reconstructed with FBP than protocol B reconstructed with FBP, irrespective of the slice level (Figure 1A). At all slice levels the image noise was also significantly higher under protocol A (Figure 1B) and there was no statistically significant difference in CNR between the protocols (Figure 1C).

In step 2, mean venous CT attenuation was significantly greater under protocol A reconstructed with HIR than protocol B reconstructed with FBP at all slice levels (Figure 2A). Image noise was also significantly lower under protocol A at all slice levels except that of the iliac vein (Figure 2B). At all levels CNR was significantly higher under protocol A (Figure 2C).

The mean CT attenuation of the pulmonary arteries was 549.4±61.1 Hounsfield units (HU) under protocol A and 503.4±62.2 HU under protocol B; it was significantly higher under protocol B (P=0.02).

### Qualitative Assessment of Image Quality

Qualitative image quality assessment results are listed in Tables 2,3. Interobserver agreement (κ) was 0.67 and 0.72 for protocol A and protocol B reconstructed with FBP, respectively, in step 1. It was 0.74 and 0.72 for protocol A reconstructed with HIR and protocol B reconstructed with FBP, respectively, in step 2. In step 1, the mean visual scores for graininess, streak artifact, depiction of abdominal organs, and overall image quality were significantly lower for protocol A, but the scores for vessel enhancement were significantly higher. In step 2 there was no statistically significant difference between the protocols in the visual scores for graininess, streak artifact, depiction of abdominal organs, and overall image quality. The mean visual score for vessel enhancement was significantly higher under protocol A. Representative cases are shown in Figures 3–5. Under both protocols a score of 4 (excellent) was given for the visual evaluation of pulmonary arterial en-

### Table 2. Qualitative Assessment of Image Quality (Step 1)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Protocol A (80 kV, FBP)</th>
<th>Protocol B (120 kV, FBP)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graininess</td>
<td>2.5±0.5</td>
<td>3.5±0.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Streak artifact</td>
<td>2.6±0.5</td>
<td>3.6±0.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Vessel enhancement</td>
<td>3.4±0.6</td>
<td>2.5±0.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Depiction of abdominal organs</td>
<td>3.0±0.5</td>
<td>3.5±0.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Overall image quality</td>
<td>2.9±0.6</td>
<td>3.3±0.7</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Data given as mean±SD.

FBP, filtered back projection.

### Table 3. Qualitative Assessment of Image Quality (Step 2)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Protocol A (80 kV, HIR)</th>
<th>Protocol B (120 kV, FBP)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graininess</td>
<td>3.5±0.5</td>
<td>3.5±0.5</td>
<td>0.79</td>
</tr>
<tr>
<td>Streak artifact</td>
<td>3.4±0.5</td>
<td>3.6±0.6</td>
<td>0.15</td>
</tr>
<tr>
<td>Vessel enhancement</td>
<td>3.4±0.6</td>
<td>2.5±0.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Depiction of abdominal organs</td>
<td>3.8±0.4</td>
<td>3.5±0.5</td>
<td>0.10</td>
</tr>
<tr>
<td>Overall image quality</td>
<td>3.5±0.5</td>
<td>3.3±0.7</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Data given as mean±SD.

FBP, filtered back projection; HIR, hybrid iterative reconstruction.
Figure 3. (A–D) A 67-year-old man and (E–H) a 63-year-old man without deep vein thrombosis examined at 4 slice levels [(A,E) inferior vena cava; (B,F) right iliac vein; (C,G) right femoral vein; and (D,H) deep vein level] in the right lower thigh under (A–D) protocol A with filtered back projection (FBP) and (E–H) protocol B with FBP. Under protocol A, venous enhancement (arrows) was stronger at all slice levels.

Figure 4. (A–D) A 61-year-old woman and (E–H) a 63-year-old man without deep vein thrombosis examined at the same sites as in Figure 3 under (A–D) protocol A with hybrid iterative reconstruction and (E–H) protocol B with filtered back projection. Under protocol A venous enhancement was stronger (arrows) and the depiction of abdominal organs was better than under protocol B.
enhancement in all patients.

Discussion

A reduction in the tube voltage yields higher vascular enhancement at a reduced radiation dose. Iodine attenuation increases as the tube voltage decreases because the mean photon energy in the X-ray beam moves closer to the k-absorption edge of iodine, resulting in an increased photoelectric effect and decreased Compton scattering that, in effect, translates into a higher mean attenuation value of iodine. In addition, the low-tube-voltage technique drastically reduces the radiation dose, which is proportional to the square of the tube voltage, although the transmitted radiation is decreased and image noise is increased. The step 1 results showed that the 80-kV protocol reconstructed with FBP (protocol A) that required a lower volume of contrast material resulted in a significant reduction in the radiation dose while it maintained CNR at CTV. The overall image quality score, however, was significantly lower than that for the 120-kV protocol (protocol B) due to increased image noise and streak artifacts.

The iterative reconstruction technique can reduce the image noise and yield higher-quality images at lower radiation doses than FBP reconstruction. Earlier investigations that used a prior-generation iterative reconstruction technique (the adaptive statistical iterative reconstruction [ASIR] algorithm) suggested that it could be used to compensate for the increased image noise produced at lower radiation-dose settings. The excessive image noise reduction achieved by ASIR, however, was not uniform across the entire spatial frequency spectrum and shifts in the noise spectrum can markedly alter the image texture. Leipsic et al, who used ASIR, suggested that highly iterative reconstructions produce images that are significantly different in appearance from images acquired with the FBP reconstruction algorithm; their noise texture appears different and their borders manifest a higher degree of smoothness resulting in a “plastic” or “artificial” appearance. HIR (iDose4), a new type of iterative reconstruction algorithm, involves an HIR technique that uses a complicated mathematical model that includes projection and image spaces. Unlike previously reported iterative reconstruction algorithms, it removes noise from the raw data by applying a Poisson noise-reduction algorithm. The data are then reviewed in pixel space, where the HIR reconstructed image is compared with an optimal noise-free anatomical model; this results in noise reduction while attempting to maintain the image quality and appearance of a full-dose image. HIR provides better noise removal efficiency across the noise spectrum and preserves the natural appearance of images.

An iterative reconstruction algorithm can be used to compensate for the increased image noise and streak produced at low-tube-voltage settings. Marin et al, who applied an ASIR algorithm at low-tube-voltage abdominal CT imaging, reported that the image quality was improved and the radiation dose was decreased. In their phantom study, Funama et al found that the combination of low-tube-voltage coronary CTA and the HIR algorithm was superior to low and standard tube-voltage coronary CTA with the FBP reconstruction algorithm for reducing the radiation dose and improving image quality. To our knowledge, the present study is the first comparative evaluation of the low tube voltage protocol reconstructed with HIR and the standard tube voltage protocol reconstructed with the FBP reconstruction algorithm at CTV.

We found that at CTV, the 80-kV protocol, which requires a lower dose of contrast material, and application of the HIR algorithm yielded a higher CNR and better image quality than the standard 120-kV protocol with the FBP algorithm. Visual evaluation showed that graininess, streak artifact, depiction of abdominal organs, and overall image quality were improved with HIR.

Although an evidence-based consensus for the addition of CTV to pulmonary CTA remains to be established, the com-
bination of CTV and pulmonary CTA is now widely used to assess patients with suspected PTE or DVT. Concerns have been raised, however, about the additional radiation exposure and the use of a larger amount of contrast material when patients are subjected to CTV. The reported effective radiation dose during CTV to the pelvis and lower extremities ranges from 2.3 mSv to 11.8 mSv.24,25 The high radiation dose during CTV is primarily due to irradiation of the pelvis.26,27 Kalva et al suggested that CTV be limited to the lower extremities because CTV of the pelvis does not significantly improve the DVT detection rate.28 The present study has shown that low-tube-voltage (80 kV) CTV of the abdomen and lower extremities reduced the radiation dose by approximately 30% compared with the standard 120-kV technique. The radiation dose during CTV should be reduced more if the scan range is limited to the lower extremities.

CTV also requires a larger amount of contrast material: 120–150 ml of iodinated contrast material at a concentration of ≥300 mgI/ml is needed to obtain adequate opacification of the veins in the pelvis and lower extremities.30–33 Larger amounts of contrast material are associated with a risk of contrast-induced nephropathy (CIN). Because the renal toxicity of iodinated contrast material is dose dependent,34 it is important to reduce the dose to decrease the risk of CIN without compromising image quality. The low-tube-voltage CTV technique lowered the required amount of contrast material by approximately 20% compared with the routine 120-kV protocol. Because there was no degradation of vessel enhancement, this may reduce the risk for CIN.

Venous ultrasonography has replaced conventional venography as the first-line diagnostic test for DVT.18 Its sensitivity and specificity for DVT in the femoral and popliteal veins is 95%–97. But this diagnostic method is not without drawbacks,38 in that it is poor at depicting the pelvic, iliac, and calf veins, is user/operator dependent, may result in false-negative findings in the case of duplicated venous anatomy; and its accuracy is also lower in asymptomatic patients.39 CTV may overcome these problems and it yields additional useful information. For example, it may indicate the presence of pelvic tumors and other abdominal organ disease and it facilitates anatomic venous evaluations performed before the inception of therapeutic measures such as the placement of inferior vena cava filters, percutaneous catheter-directed thrombolysis, and rheolytic thrombectomy.40

The present study has some limitations. Compared to Western subjects, the Japanese patients had a relatively low body weight (mean, 61.5±12.2 kg; range, 38–83 kg). In large-bodied patients, low-tube-voltage scans tend to be of poorer quality due to increased image noise attributable to radiation scattering and absorption especially in the pelvis. When we defined inadequate image quality as image noise >20 HU, we found that the image quality was poor in 2 patients who weighed ≥75 kg and who were underwent the 80-kV protocol with HIR. In contrast, under the same protocol, the quality of images was acceptable in all patients weighing <75 kg, suggesting that the 80-kV protocol with HIR is suitable only in lower-weight patients. The acquisition of scans at 100 kV may help to counterbalance the increased image noise encountered in patients weighing ≥75 kg.

We did not evaluate diagnostic performance with regard to the detection of DVT because not all patients underwent ultrasonography and conventional venography, and no reference standard for DVT was available. We also did not assess the ability to diagnose PTE; instead, we evaluated the quality of images acquired at pulmonary CTA. Based on earlier reports,31,42 we routinely use a low-tube-voltage technique at pulmonary CTA. In the current study, mean CT attenuation in the pulmonary arteries was significantly lower under protocol A although, compared to those reports, we obtained higher pulmonary artery enhancement under protocol A. Moreover, visual evaluation of pulmonary arterial enhancement showed that the acquired images were sufficient for diagnosis.

Conclusion

CTV with FBP at a tube voltage of 80 kV instead of 120 kV allows for an up to 30% reduction in the radiation dose and a decrease in the contrast material dose by approximately 20% while maintaining the CNR. Furthermore, application of the HIR algorithm at 80-kV venography significantly improved the quality of images compared to images acquired at 120 kV with the FBP algorithm. Based on the observations reported here we recommend the combination of low-tube-voltage CTV with the HIR technique in patients with suspected PTE and DVT.

References


