INTRODUCTION

The widespread use of computed tomography (CT) raises concerns about the hazards of contrast material exposure. Contrast-induced nephropathy (CIN) is common; it occurs in 2–12% of patients after they undergo contrast-enhanced CT (1, 2). CIN accounts for approximately 10% of the cases of hospital-acquired renal failure and is associated with increases in morbidity, mortality, medical expenses, and length of hospital stay (3, 4). Many reports have suggested that total iodine load correlates well with the risk of CIN development (5, 6). Furthermore, a recent guideline from European Society of Urogenital Radiology recommends the volume of contrast material to be reduced for the prevention of CIN (7). Because kidney CT is indicated for patients with suspected renal pathology, which is a main risk factor for CIN development, the kidney CT protocol should specify the smallest amount of diagnostically appropriate iodine-based contrast material.

Although it may be simple to use a small volume or low-concentration contrast material in practice, the resulting decrease in CT attenuation can lower image quality and affect diagnostic accuracy. One possible solution is iterative reconstruction (IR), which reduces image noise without compromising spatial resolution and, hence, has started to replace filtered back projection.
Small Contrast Volume CT

(FBP), the conventional reconstruction method and still commonly used in developing countries (8). Iterative Model Reconstruction (IMR; Philips Healthcare, Cleveland, OH, USA) is a recent knowledge-based IR system that, by using accurate system models, results in 70–83% less image noise than does FBP (9, 10). If we apply both IR and a small contrast volume in the kidney CT protocol, we may acquire acceptable-quality CT images and reduce the patient’s total iodine load, which may be beneficial for those at risk of CIN development. However, to control other anthropological factors which may affect image quality and to avoid the harm of radiation exposure, a preliminary study that uses an animal model is appropriate.

Therefore, the aim of our study was to investigate the use of IR and a small volume of contrast material for kidney CT in a rabbit model. We compared the subjective and objective image qualities of two CT protocols: 1) small contrast volume with IR and 2) conventional contrast volume with FBP reconstruction.

MATERIALS AND METHODS

This prospective study was approved by the Institutional Animal Care and Use Committee at our institution, and we complied with the National Institutes of Health guidelines for use of laboratory animals (16-0092-S1AO).

Image Acquisition

Twenty adult male New Zealand white rabbits that weighed 2.8–3.3 kg were included in this study. At the first week, 20 rabbits were randomly assigned to constitute 10 of the study group and the other 10 of the control group and underwent kidney CT using 350 mgI/mL of contrast material. The amount of contrast material in two groups were determined based on prior studies and our pilot study (11-13). In the study group, 4 mL of contrast material was administered and images were reconstructed with IMR. In the control group, 6 mL of contrast material was injected and images were reconstructed with FBP. One week later, 20 rabbits were randomly assigned to the study and control groups and the same design study was repeated except usage of 240 mgI/mL contrast material.

Before undergoing CT, the rabbits were anesthetized with an intramuscular injection of 5 mg/kg-body weight of 2% xylazine hydrochloride (Rompun; Bayer, Seoul, Korea). A 22-gauge intravenous catheter was inserted into the marginal ear vein for the administration of contrast material.

All CT scans were performed at the same 64 channel CT scanner (IQon CT; Philips Medical Systems, Bothell, WA, USA). The kidney CT protocol consisted of a pre-contrast phase and four dynamic phases, as did our previous rabbit kidney CT protocol (14). The scan range was 12 cm starting from the level of the 10th thoracic vertebra body superior endplate. We used the bolus tracking technique, and the first contrast-enhanced scan was acquired 5 seconds (s) after the attenuation value reached 100 Hounsfield units in the abdominal aorta at the uppermost slice. Images were subsequently scanned at 15 s and 35 s for the corticomedullary phase, and at 65 s for the nephrographic phase.

For the study group, 4 mL of contrast material and 2 mL of normal saline flush were injected, whereas for the control group, 6 mL of contrast material was administered. Thus, in both groups a total 6 mL of different preparation of contrast material was applied. A power injector (Envision CT injector; Medrad, Indianola, PA, USA) was used to administer aforementioned contrast material preparation to each rabbit at the same rate of 0.3 mL/s. In the first experiment, 350 mgI/mL contrast material (Iversense 350; Taejoon Pharm, Seoul, Korea) was used. One week later, the procedure was repeated with 240 mgI/mL contrast material (Iversense 240; Taejoon Pharm). Hence, there were four combinations of CT images according to contrast material concentration and volume; one set of CT images was acquired for each combination.

The specific CT scan parameters were as follow: detector collimation, 0.625 × 64 mm; scan field of view, 137 × 137 mm; rotation time, 0.33 s; beam pitch, 0.7; slice thickness, 3 mm with 3 mm intervals; and reconstruction intervals of 1 mm. We used a fixed 80 kVp for the CT scan because the size and body weight of the rabbits were comparable to those of a neonate (15). Both angular and z-axis automatic tube current modulation were applied by using automatic exposure control (DoseRight; Philips Healthcare) with a reference Dose Right Index level of 8. In our study, the axial and coronal images were reconstructed for each dynamic phase by using FBP for the control group and IMR level 1 with medium sharpness for the study group.
Qualitative Image Analysis

Image quality was quantitatively and qualitatively analyzed by consensus of two radiologists (and, 11 and 21 years of experience in genitourinary imaging, respectively) who were blinded to the CT protocol information. After the randomization of the four CT datasets, the reviewers graded qualitative parameters on a 4-point scale in consensus. Qualitative image parameters such as sharpness, noise, texture and presence of streak artifacts were evaluated based on the criteria suggested from previous literatures (16-23).

Since the main role of kidney CT is detection of any abnormality along the urinary tract, the image sharpness of the urinary tract contours was determined (1, blurry; 2, poorer than average; 3, better than average; and 4, sharpest). Severe image noise or streak artifact may hinder accurate interpretation of CT image, especially the latter in the nephrographic phase has been reported not uncommon in previous study (23). Thus, image noise and streak artifacts were categorized (1, image noise/streak artifacts present and unacceptable; 2, image noise/streak artifacts present and interfering with visualization of adjacent structures; 3, image noise/streak artifacts present but not interfering with visualization of adjacent structures; and 4, minimal or no noise/artifacts). The image texture was graded as previous literature which reported a pixelated image texture are common in knowledge-based IR (1, blocky appearance or change affecting diagnostic confidence; 2, perceptible change; 3, no noticeable change after changing the window setting; and 4, no noticeable change) (19-22).

Quantitative Image Analysis

The same two reviewers manually drew circular regions of interests (ROIs) at each anatomical structure to determine the CT attenuation values in consensus. When drawing ROIs, homogeneous areas were selected and vessels, fat infiltration, prominent artifacts, and areas of focal changes in parenchymal attenuation were carefully avoided. Each side of kidney was considered independently and all of the measurements were conducted twice and the average value was used for statistical analysis. The reviewers measured the CT attenuations of the renal cortex, outer medulla, and inner medulla at the corticomedullary phases and those of the renal pelvis at the nephrographic phase (Fig. 1). For quantitative analysis, the parameters of CT attenuation, image noise, signal-to-noise ratio (SNR), contrast-to-noise ratio (CNR), and figure of merit (FOM) were compared between two groups based on the criteria suggested from previous literatures (24-28). At each dynamic phase, the standard deviation of the CT attenuation value of the paraspinal muscles was defined as the image noise. The SNR was calculated by dividing the CT attenuation value of the corresponding anatomical structure by the image noise. Since higher value of SNR does not guarantee higher CNR, we independently measured CNR (24). The CNR was calculated as:

\[ \text{CNR} = \frac{\text{mean} \text{CT value of structure}}{\text{SD of image noise}} \]

Fig. 1. Representative axial images showing four region-of-interest circles inside kidney at 35 s (A) and 65 s (B). The CT attenuation values were measured at the renal cortex, outer medulla, inner medulla, and renal pelvis. The 35 s (A) image is displayed at the window width of 900 HU and level of 450 HU and the 65 s (B) image is displayed at the window width of 500 HU and level of 350 HU. HU = Hounsfield units.
was determined by subtracting the CT attenuation value of the paraspinal muscles from that of corresponding anatomical structure and dividing this difference by the image noise (25).

To compensate for the differences in tube currents and radiation doses among the CT scans, we evaluated the FOM as the ratio of CNR2 to the effective radiation dose. Since CNR2 is proportional to the radiation dose, the FOM values enable the comparison of CNR independent of the tube current and radiation dose (26, 27). To convert the dose-length product into an effective radiation dose, we used a conversion factor of 0.0485, which is the mean value of neonate male and female considering comparable body volume and weight to those of rabbit in our study (28).

**Statistical Analysis**

The independent t-test and Mann-Whitney U test were applied to compare the subjective and objective image qualities between two groups, as appropriate. A p-value less than 0.05 indicated statistical significance. All statistical analysis was performed by using a software package (SPSS Statistics for Windows, Version 21.0; IBM Corp., Armonk, NY, USA).

**RESULTS**

**Qualitative Analysis**

Comparison of qualitative image quality is summarized in Table 1. At all dynamic phases, the study group images were sharper and had less noise than the corresponding control group images (all, \( p < 0.05 \)). The study group scores for streak artifacts were lower for 65 s phases in both concentration of contrast material (both, \( p < 0.05 \)). However, the image texture was worse in all of the study group images (all except one, \( p < 0.05 \)), other than the image obtained at 5 s with 240 mg/mL contrast material (\( p = 0.063 \)). Although there were few exceptions, those results tended to be consistent regardless of the contrast material concentration and dynamic phases.

The qualitative image scores of the study group given the 350 mg/mL contrast material and those of the one given the 240

| Qualitative Parameters | 350 mg/mL | 240 mg/mL | \( p \)-Value 1* | \( p \)-Value 2† | \( p \)-Value 3‡ |
|------------------------|-----------|-----------|----------------|----------------|----------------|
| **5 s**                |           |           |                |                |                |
| Image sharpness        | 2.8 ± 0.4 | 1.7 ± 0.5 | 2.4 ± 0.8      | 1.2 ± 0.4      | < 0.000        | < 0.000        | 0.143          |
| Image noise            | 2.9 ± 0.3 | 1.7 ± 0.5 | 2.3 ± 0.8      | 1.5 ± 0.5      | < 0.000        | < 0.000        | 0.999          |
| Image texture          | 2.5 ± 0.5 | 3.8 ± 0.4 | 3.3 ± 0.7      | 3.7 ± 0.5      | < 0.000        | 0.063          | 0.023          |
| Streak artifacts       | 4.0 ± 0.0 | 4.0 ± 0.0 | 4.0 ± 0.0      | 4.0 ± 0.0      | 0.999          | 0.999          | 0.999          |
| **15 s**               |           |           |                |                |                |
| Image sharpness        | 2.9 ± 0.3 | 1.9 ± 0.3 | 2.8 ± 0.4      | 1.7 ± 0.5      | < 0.000        | < 0.000        | 0.739          |
| Image noise            | 2.9 ± 0.3 | 2.0 ± 0.0 | 3.0 ± 0.0      | 1.9 ± 0.3      | < 0.000        | < 0.000        | 0.739          |
| Image texture          | 2.7 ± 0.5 | 3.8 ± 0.4 | 3.3 ± 0.5      | 3.9 ± 0.3      | < 0.000        | 0.023          | 0.052          |
| Streak artifacts       | 4.0 ± 0.0 | 4.0 ± 0.0 | 4.0 ± 0.0      | 4.0 ± 0.0      | 0.999          | 0.999          | 0.999          |
| **35 s**               |           |           |                |                |                |
| Image sharpness        | 2.7 ± 0.7 | 2.0 ± 0.0 | 2.7 ± 0.5      | 1.8 ± 0.4      | 0.007          | 0.003          | 0.796          |
| Image noise            | 3.0 ± 0.0 | 2.1 ± 0.3 | 3.0 ± 0.0      | 2.0 ± 0.0      | < 0.000        | < 0.000        | 0.999          |
| Image texture          | 2.0 ± 0.0 | 3.9 ± 0.3 | 2.1 ± 0.6      | 4.0 ± 0.0      | < 0.000        | < 0.000        | 0.739          |
| Streak artifacts       | 3.7 ± 0.5 | 3.3 ± 0.5 | 4.0 ± 0.0      | 3.5 ± 0.5      | 0.143          | 0.063          | 0.280          |
| **65 s**               |           |           |                |                |                |
| Image sharpness        | 2.9 ± 0.3 | 2.0 ± 0.0 | 2.9 ± 0.3      | 1.8 ± 0.4      | < 0.000        | < 0.000        | 0.999          |
| Image noise            | 3.0 ± 0.0 | 2.1 ± 0.3 | 2.9 ± 0.3      | 2.0 ± 0.0      | < 0.000        | < 0.000        | 0.739          |
| Image texture          | 2.6 ± 0.5 | 3.9 ± 0.3 | 3.2 ± 0.6      | 4.0 ± 0.0      | < 0.000        | 0.007          | 0.075          |
| Streak artifacts       | 3.8 ± 0.4 | 2.9 ± 0.3 | 3.9 ± 0.3      | 3.1 ± 0.6      | 0.001          | 0.005          | 0.739          |

Unless otherwise specified, data are presented as mean ± standard deviation.

*Comparison between the study and control groups given 350 mg/mL contrast material.
†Comparison between the study and control groups given 240 mg/mL contrast material.
‡Comparison between the study group given 350 mg/mL contrast material and the study group given 240 mg/mL contrast material.
mgI/mL contrast material were not different aside from one case (all except one, $p > 0.05$). The image texture was worse in the images obtained at 5 s in the 350 mgI/mL group ($p = 0.023$).

Representative 35 s and 65 s images are shown in Figs. 2, 3, respectively.

Quantitative Analysis

CT Attenuation Values

Table 2 shows comparison of CT attenuations values between groups. The CT attenuation values at the renal cortex on 15 s and 35 s were not different between the study and control groups with the same contrast material, excluding one case (all except one, $p > 0.05$). However, the CT attenuation values of the outer medulla at 15 s and 35 s as well as those of the inner medulla at 15 s were lower in the study group (all, $p < 0.05$). The CT attenuation values of the inner medulla at 35 s and the renal pelvis at 65 s were not different between the groups of the same contrast material (all, $p > 0.05$). Between the two study groups with different contrast concentration, higher enhancement degree was noted in the patients given the 350 mgI/mL solution than in those given the 240 mgI/mL solution (all except one, $p < 0.05$).

Image Noise And Radiation Dose

Table 3 shows the specific data. The mean value of image noise was lower in the study group than in the control group for both
Fig. 3. Representative axial images of left kidney obtained at 65 s for each group. The images of the control groups given 350 mgI/mL contrast material (B) and 240 mgI/mL contrast material (D) show noticeable streak artifacts that extend to the periphery of the kidney parenchyma (arrowheads). However, the images of the study groups given 350 mgI/mL contrast material (A) and 240 mgI/mL contrast material (C) depict well-defined boundaries of intrarenal structures and negligible streak artifacts. All of the images are displayed with the same window width of 500 HU and level of 350 HU settings.

HU = Hounsfield units

Table 2. Comparison of the CT Attenuation Values at the Renal Structures

|                    | 350 mgI/mL | 240 mgI/mL | p-Value 1* | p-Value 2† | p-Value 3‡ |
|--------------------|------------|------------|------------|------------|------------|
|                    | Study (HU) | Control (HU) | Study (HU) | Control (HU) |           |
| Renal cortex       |            |            |            |            |            |
| 15 s               | 531 ± 110  | 557 ± 73   | 373 ± 68   | 389 ± 75   | 0.390      |
| 35 s               | 255 ± 28   | 313 ± 54   | 215 ± 39   | 222 ± 32   | < 0.000    |
| Outer medulla      |            |            |            |            |            |
| 15 s               | 227 ± 33   | 176 ± 32   | 155 ± 25   | 220 ± 34   | < 0.000    |
| 35 s               | 508 ± 46   | 557 ± 71   | 406 ± 58   | 465 ± 70   | 0.019      |
| Inner medulla      |            |            |            |            |            |
| 15 s               | 80 ± 9     | 92 ± 21    | 76 ± 8     | 82 ± 4     | 0.027      |
| 35 s               | 819 ± 110  | 773 ± 194  | 699 ± 128  | 695 ± 135  | 0.356      |
| Renal pelvis       |            |            |            |            |            |
| 65 s               | 1111 ± 501 | 1142 ± 453 | 699 ± 128  | 645 ± 284  | 0.842      |

Unless otherwise specified, data are presented as mean ± standard deviation.

*Comparison between the study and control groups given 350 mgI/mL contrast material.
†Comparison between the study and control groups given 240 mgI/mL contrast material.
‡Comparison between the study group given 350 mgI/mL contrast material and the study group given 240 mgI/mL contrast material.

HU = Hounsfield units
contrast material concentration (both, \( p < 0.000 \)). Between the two study groups, the image noise of the group given the 240 mgI/mL solution was lower than that given the 350 mgI/mL solution (\( p < 0.000 \)). Irrespective of contrast material volume and concentration, the mean effective radiation dose were not different between compared groups (all, \( p > 0.05 \)).

Comparison of SNR, CNR, and FOM

Fig. 4 contain box-and-whisker plots of each dynamic phase for comparisons of SNR, CNR, and FOM between groups according to the contrast material volume and concentration. At all dynamic phases, the SNR, CNR, and FOM of each anatomical structure were higher in the study group than the control group (all, \( p < 0.05 \)).

DISCUSSION

In our study, all the qualitative parameters excluding image texture were better among images obtained with a small volume of contrast material than among those obtained with the conventional volume. The overall CT attenuation values at the intrarenal structures in the study group were lower than or similar to those in the corresponding control group. However, because the reduction in image noise from IR was greater than the decrease in CT attenuation value, other quantitative image parameters of SNR, CNR, and FOM were considerably higher in the study group. Our findings suggest that the noise reduction resulting from a knowledge-based IR algorithm could compensate for lower CT attenuation values and allow for better overall

Table 3. Comparison of Image Noise and Radiation Dose

|                  | 350 mgI/mL | 240 mgI/mL | \( p \)-Value 1* | \( p \)-Value 2† | \( p \)-Value 3‡ |
|------------------|------------|------------|------------------|------------------|------------------|
|                  | Study      | Control    | Study           | Control          |                  |
| Image noise      | 3.96 ± 0.9 | 9.35 ± 1.1 | 3.18 ± 0.6       | 8.84 ± 0.9       | < 0.000          |
| Effective dose (mSv) | 2.83 ± 0.1 | 2.78 ± 0.2 | 2.71 ± 0.2       | 2.69 ± 0.1       | 0.105            |

Unless otherwise specified, data are presented as mean ± standard deviation.

*Comparison between the study and control groups given 350 mgI/mL contrast material.
†Comparison between the study and control groups given 240 mgI/mL contrast material.
‡Comparison between the study group given 350 mgI/mL contrast material and the study group given 240 mgI/mL contrast material.

Fig. 4. Box-and-whisker plots show comparisons of the SNR, CNR, and FOM values of each intrarenal structure according to dynamic phase and contrast material concentration. Ends of boxes are 25th and 75th quartiles and lines across middles of boxes are medians. Maximum and minimum values are displayed with whiskers connecting points to center box. During the corticomedullary phase of 15 s, the median values of SNR (A), CNR (B), and FOM (C) at each intrarenal structure are higher in the study group than in the control group, regardless of contrast material concentration. During subsequent nephrographic phase of 65 s, the quantitative image parameters of SNR (D), CNR (E), and FOM (F) are better in the study group than in the control group for both contrast material concentration.

CNR = contrast-to-noise ratio, FOM = figure of merit, SNR = signal-to-noise ratio
image quality even with a smaller volume of contrast material.

In general, our findings are consistent with previous studies that have reported that the application of IR with a low peak voltage can produce acceptable image quality with the advantages of a smaller volume of contrast material and a lower radiation dose in abdominal CT imaging (11-13, 29). Since the minimum peak voltage setting provided by the CT scanner was 80 kV, we cannot further reduce the peak voltage in our study. Thus, our fixed 80 kVp setting for all groups resulted in similar radiation doses.

Since the kidney serves unique excretion function including the contrast material, it may affect the enhancement and arti-
fact pattern in the kidney CT. Concentrated urine in the pelvocalyceal system during the nephrographic phase is a major source of streak artifacts, which may limit the evaluation of the kidney parenchyma and focal lesions (23). Under low tube voltage, streak artifacts are more prominent because the penetration by X-ray photons is reduced (30). In our study, the study group images of nephrographic phase showed negligible streak artifacts in both contrast material concentration; this finding suggests that IR may suppress streak artifacts despite the low 80 kVp setting (Fig. 3). As streak artifacts result from corrupt sinogram patterns due to lack of projection data, IR has been shown to effectively suppress these streak artifacts, which is consistent with our study result (22, 31, 32).

One disadvantage of IR is that it yields an unnaturally blocky image appearance; this finding has been reported several times (19-22). Images were especially pixelated at 35 s of the corticomedullary phase in our study when the primary purpose is the differentiation of adjacent intrarenal structures. Although a blocky image appearance itself does not indicate poor image sharpness, unfamiliarity with this image texture may influence the judgment of radiologists. Thus, future research is needed to assess how unnatural pixelated image texture affects diagnostic accuracy.

This study has several limitations. First, we examined normal kidneys and evaluated the quality of CT images. Since the CT attenuation value, the degree and timing of enhancement are different from those of conventional kidney CT, further research with a disease phantom model would be desirable to evaluate the diagnostic accuracy of this CT protocol (33, 34). Second, we evaluated the effects of contrast material volume and concentration in isolation; however, other contrast material-related factors, such as injection rate or split bolus method, could also be further optimized to acquire better image quality. Similarly, since we used the same CT scanner in our study, thus other CT scanner-related factors which may influence the image quality was not examined, although, it is beyond the scope of our study. Finally, even though we decided the criteria of qualitative analysis based on previous literatures, the inherent limitation of subjectivity remains in our study.

In conclusion, the use of IR and a small volume of contrast material yielded CT images with better objective and subjective qualities compared to those obtained with FBP and the conventional contrast volume in a rabbit model.

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반복적 재구성 기법과 저용량 조영제를 이용한 토끼 신장 CT: 기존 영상과의 비교연구

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목적: 본 연구에서는 반복적 재구성 기법과 저용량 조영제를 사용한 토끼 신장 CT 영상의 질을 비교 평가하고자 하였다.

대상과 방법: 실험에 사용된 토끼는 총 20마리로서, 실험군에서는 4 mL의 조영제와 반복적 재구성 기법을 적용하였고, 대조군에서는 6 mL의 조영제와 여과 역투사법을 이용하였다. CT영상의 질 평가는 2명의 비뇨영상의학 전문의의 합의로 이루어졌다. 영상의 선예도, 영상 잡음, 영상 질감, 줄무늬 인공물의 4가지 항목을 정성적으로 평가하였다. 정량적 평가 항목으로는 평균 CT 감쇄 값, 영상 잡음, 신호 대 잡음비, 대조도 대 잡음비 및 성능 지수를 계산하였다.

결과: 정성적 비교 평가 결과, 실험군에서 유의하게 영상 질감이 향상되어 향상되었고 보다 나은 영상의 선예도를 보여 주었다(\(p < 0.05\)). 하지만, 영상의 질감은 실험군에서 오히려 떨어졌다(\(p < 0.05\)). 평균 CT 감쇄 값은 실험군과 대조군이 비슷하였지만 실험군에서 영상 잡음이 현저하게 낮아 신호 대 잡음비, 대조도 대 잡음비 및 성능 지수 모두 대조군에 비해 유의하게 높은 값을 보였다(\(p < 0.05\)).

결론: 4 mL 조영제와 반복적 재구성 기법을 적용한 토끼 신장 CT는 기존의 6 mL 조영제와 여과 역투사법을 사용한 CT 보다 나은 영상의 질을 보여주었다.

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