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Reduced iodinated contrast media for abdominal imaging by dual-layer spectral detector computed tomography for patients with kidney disease

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ABSTRACT

Contrast-enhanced computed tomography using iodinated contrast media is useful for diagnosis of gastrointestinal diseases. However, contrast-induced nephropathy remains problematic for kidney diseases patients. Although current guidelines recommended the use of a minimal dose of contrast media necessary to obtain adequate images for diagnosis, obtaining adequate images with sufficient contrast enhancement is difficult with conventional computed tomography using reduced contrast media. Dual-layer spectral detector computed tomography enables the simultaneous acquisition of low- and high-energy data and the reconstruction of virtual monochromatic images ranging from 40 to 200 keV, retrospectively. Low-energy virtual monochromatic images can enhance the contrast of images, thereby facilitating reduced contrast media. In case 1, abdominal computed tomography angiography at 50 keV using 40% of the conventional dose of contrast media revealed the artery that was the source of diverticular bleeding in the ascending colon. In case 2, ischemia of the transverse colon was diagnosed by contrast-enhanced computed tomography and iodine-selective imaging using 40% of the conventional dose of contrast media. In case 3, advanced esophagogastric junctional cancer was staged and preoperative abdominal computed tomography angiography could be obtained with 30% of the conventional dose of contrast media. However, the texture of virtual monochromatic images may be a limitation at low energy.

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Introduction

Contrast-enhanced computed tomography (CECT) with administration of iodinated contrast media is used worldwide in routine practice to diagnose various gastrointestinal diseases. However, contrast-induced nephropathy (CIN) remains problematic for patients with kidney disease. A previous report revealed that the incidence of CIN among patients with a baseline estimated glomerular filtration rate (eGFR) of 45-59 mL/min/1.73 m^2 was 0%, whereas a rate of 30-44 mL/min/1.73 m^2 was 2.9%, and <30 mL/min/1.73 m^2 was 12.1% [1]. Available guidelines use a baseline eGFR of < 45 mL/min/1.73 m^2 as a cutoff for the risk of CIN after CECT [2,3]. In Japan, the incidence of chronic kidney disease is among the highest in the world because a Japanese person has, on average, a much lower nephron count than a Westerner because of the smaller body size and various genetic factors [4]. Therefore, CIN caused by CECT is a crucial problem, especially in countries with higher incidences of chronic kidney disease, such as Japan.

Intravenous administration of an isotonic solution, such as physiological saline or sodium bicarbonate, both before and after CECT has been shown to reduce the incidence of CIN. Furthermore, available guidelines recommend the minimal use of contrast media necessary to obtain adequate images for diagnosis [2,3]. However, in contrast to conventional computed tomography (CT), which provides only 120-kVp images corresponding to 70-keV, the contrast enhancement of CECT images acquired with minimal use of contrast media is insufficient for diagnosis.

Dual-layer spectral detector CT, which was first commercially available in 2016, employs 1 X-ray source and dual-layer detectors, with the upper layer collecting low-energy data and the deeper layer collecting high-energy data of the emitted spectrum [5]. This novel technique enables the simultaneous acquisition of low- and high-energy data. Furthermore, retrospective spectral analysis of virtual monochromatic imaging with photon energy levels of 40-200 keV and iodine-selective imaging can be immediately performed on demand. Virtual monochromatic images acquired at low energy by dual-layer spectral detector CT can enhance the contrast of images, thereby facilitating a reduction in the amount of contrast media. A past report that compared image quality in dual-layer spectral detector CT revealed that 50-keV images achieved the same contrast-to-noise ratio (CNR) as a 120-kVp image with a 2.5-fold reduction in iodine concentration and 40-keV virtual monochromatic images achieved the same CNR as a 120-kVp image with a 4.0-fold reduction in iodine concentration [6]. Therefore, virtual monochromatic imaging with a low-energy dual-layer spectral detector requires less contrast media, which can prevent the incidence of CIN. However, few studies have investigated the utility of dual-layer spectral detector CT from the viewpoint of reduced contrast media for patients with an eGFR of <45 mL/min/1.73 m^2 and gastrointestinal diseases. Here we report the utility and limitations of the use of a dual-layer spectral detector for CECT with minimal iodinated contrast media for 3 patients with gastrointestinal diseases and an eGFR of <45 mL/min/1.73 m^2.

Case report

CECT was performed using a dual-layer spectral detector CT scanner (IQon Spectral CT; Philips, Health Care, Best, The Netherlands) for 3 patients with an eGFR < 45 mL/min/1.73 m^2 and gastrointestinal diseases. Iopamidol at concentrations of 300 or 370 mg I/mL (Iopamiron-300 or -370; Bayer Healthcare, Osaka, Japan) was used as the contrast medium in the present report. These dosages of iodinated contrast media were 30%–40% of the amount recommended for conventional abdominal dynamic CT at 120 kVp of 600 mg/kg. CIN was prevented in all 3 cases reported.

Case 1

An 87-year-old man with a history of diabetic nephropathy was referred to the emergency room of our hospital for treatment of bloody stools. On admission, his systolic and diastolic blood pressures were 160 and 84 mm Hg, respectively. Although no abdominal pain was revealed on physical examination, fresh bloody stool was observed on a rectal examination. As shown by the laboratory data on admission listed in Table 1 (case 1), the eGFR was low at 30.1 mL/min/1.73 m^2. Blood sugar was 3.1 mmol/L, and HbA1c-NGSP was 5.5%. Immediately after hospitalization, because the patient had massive bloody stools, CECT was performed using a dual-layer spectral detector and a contrast media dose of 40% of the conventional dose (iodine concentration of 245 mg/kg with 41 mL of iopamiron-300) to assess extravasation in the gastrointestinal tract. Extravasation

Table 1 – Laboratory data on hospital admission for cases 1, 2, and 3.

	Case 1	Case 2	Case 3
Hematology			
WBC, $\times10^9$/L	9.9	2.9	6.5
RBC, $\times10^{12}$/L	2.62	4.35	2.81
Hb, g/L	80	130	92
Plt, $\times10^6$/L	154	143	215
Blood chemistry			
TP, g/L	44	44	63
Alb, g/L	20	17	35
AST, IU/L	15	102	17
ALT, IU/L	11	30	17
LDH, IU/L	218	401	142
T-bil, μmol/L	18.8	22.2	8.6
BUN, mmol/L	14.4	10.9	6.0
Cre, μmol/L	150.3	123.8	212.2
eGFR, mL/min/1.73 m^2	30.1	43.9	22.1
CK, IU/L	N.A.	6048	N.A.
Na, mEq/L	140	141	140
K, mEq/L	3.5	3.4	3.9
Cl, mEq/L	108	110	105
Serology			
CRP, nmol/L	N.A.	3380	N.A.

WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; Plt, platelet; TP, total protein; Alb, albumin; AST, aspartate aminotransferase; ALT, alanine transaminase; BUN, blood urea nitrogen; Cre, creatinine; eGFR, estimated glomerular filtration rate; CK, creatine kinase; Na, sodium; K, potassium; Cl, chlorine; CRP, C-reactive protein; N.A., not available.

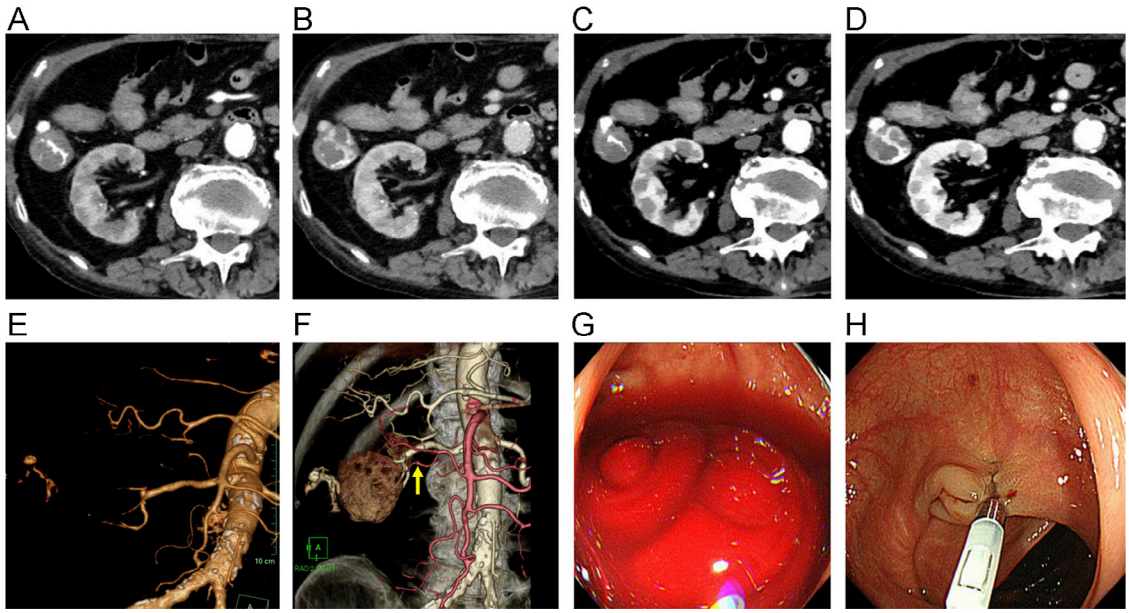

Fig. 1 – Contrast media at 40% of the conventional dose was used. (A, B) 120-kVp image. (A) Arterial phase. (B) Portal phase. Extravasation of diverticular bleeding in the ascending colon, which spread from the arterial to portal phase, was revealed. (C, D) 50-keV image. (C) Arterial phase. (D) Portal phase. Extravasation of diverticular bleeding in ascending colon was revealed. Contrast enhancement was increased, as compared with 120-kVp images. (E) Abdominal CT angiography at 120 kVp. The arterial bleeding source was not identified. (F) Abdominal CT angiography at 50 keV. The arterial bleeding source was identified clearly (yellow arrow). G, H: endoscopic findings. (G) Diverticular bleeding in the ascending colon was revealed. (H) Diverticular bleeding in the ascending colon was stopped by clipping.

of diverticular bleeding in the ascending colon, which spread from the arterial phase to the portal phase, was revealed by CECT both on 120-kVp images (Fig. 1A, B) and virtual monochromatic images at 50 keV (Fig. 1C, D). Reconstructed abdominal CT angiographic images were prepared for transcatheter arterial embolization (TAE). Although not identified at 120 kVp (Fig. 1E), CT angiography at 50 keV clearly revealed the source of arterial bleeding with a reduced amount of contrast media (Fig. 1F). Fortunately, hemostatic treatment was successful endoscopically, thus TAE was not necessary (Fig. 1G, H).

Case 2

A 49-year-old man was referred to a hospital near his home for treatment of high fever, abdominal pain, and diarrhea. His medical history included eosinophilic granulomatosis with polyangiitis, which was treated with a glucocorticoid administered at 10 mg/day. Infectious enteritis was suspected and treated with medications. However, his condition worsened and he was transferred to our hospital 3 days later in a state of impaired consciousness (Glasgow Coma Scale score, 12 points; eye opening response, 3 points; orientation, 4 points; and motor response, 5 points). His vital signs on admission were as follows: body temperature, 39.3°C; systolic blood pressure, 90 mm Hg; diastolic blood pressure, 60 mm Hg; heart rate, 148 bpm; and respiratory rate, 24 breaths/min. As shown by the laboratory data listed in Table 1 (case 2), eGFR was low at 43.9 mL/min/1.73 m^2, C-reactive protein (CRP) and serum creatine kinase levels were markedly increased at 3380 nmol/L and 6048 IU/L, respectively; immunoglobulin E was 6790 IU/L and myeloperoxidase antineutrophil cytoplasmic antibodies were <1.0 U/mL. Arterial blood gas analysis revealed a pH of 7.56, $PaCO_2$ of 14.1 mm Hg, PaO_2 of 64.3 mm Hg, and HCO_3 of 12.4 nmol/L. Because septic shock caused by bowel ischemia was suspected based on these findings, CECT was performed using a dual-layer spectral detector with reduced contrast media of 40% the conventional dosage (iodine concentration of 250 mg/kg with 45 mL of iopamiron-370). There were no findings of thinning or thickening of the bowel wall, gas in the portal vein, or ascites by nonenhanced CT (Fig. 2A). Although the arterial phase of enhanced CT images at 120 kVp (Fig. 2B) and 50 keV (Fig. 2C) showed hypoenhancement of the transverse colon wall, the same portion showed improved enhancement in the portal phase at 120 kVp (Fig. 2D) and 50 keV (Fig. 2E). These findings were more conspicuous on 50-keV images. Iodine-selective imaging showed an iodine content of 0.6 mg/mL in the transverse colon, which suggested severe hypoperfusion, and an iodine content of 2.5 mg/mL in the nonischemic bowel (Fig. 2F). There was no indication of bowel obstruction. Hence, septic shock caused by severe hypoperfusion of the transverse colon was suspected. Although blood flow in the transverse colon was severely hypoperfuse on CECT, a little blood flow remained, thus the transverse colon had not yet become necrotic. Since there was a chance that the blood flow could recover by improving blood pressure with infusion, the patient was treated in the intensive care unit according to the Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016 [7]. After intensive care, his condition

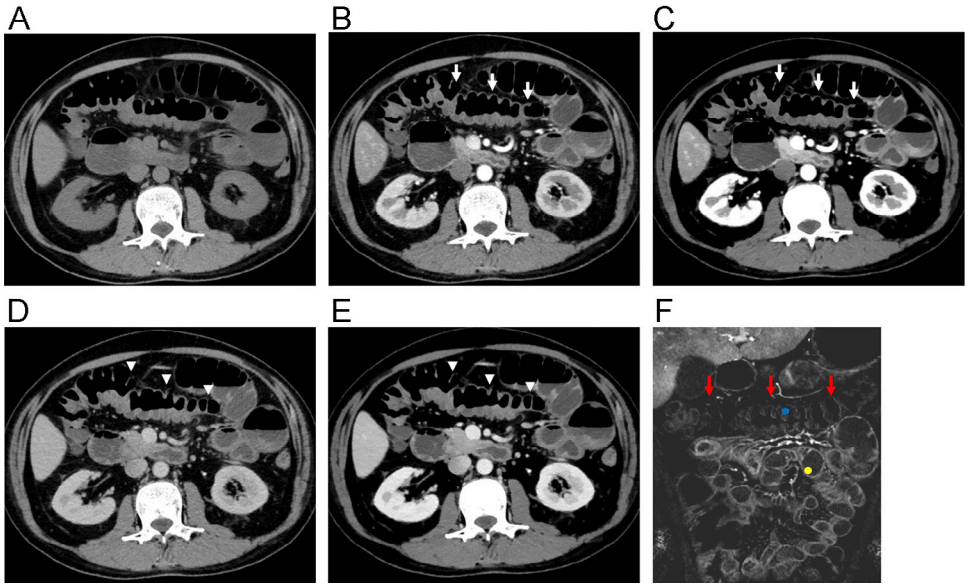

Fig. 2 – Contrast media of 40% of the conventional dose was used. (A) Nonenhanced 120-kVp image. There were no findings of thinning or thickening of the bowel wall, gas in the portal vein, or ascites. (B,C) Arterial phase. (B) 120-kVp image. (C) 50-keV image. Hypoenhancement of the transverse colon wall is shown (white arrows). This finding was more conspicuous on a 50-keV image than a 120-kVp image. (D,E) Portal phase. (D) 120-kVp image. (E) 50-keV image. Contrast enhancement was improved, as compared with the arterial phase (white arrow heads). (F) Iodine-selective image. The transverse colon is indicated with a red arrow. Iodine content of 0.6 mg/mL in the transverse colon (blue dot) suggested severe hypoperfusion and an iodine content of 2.5 mg/mL in the non-ischemic bowel (yellow dot).

improved and he was discharged 17 days after admission without surgical treatment.

Case 3

A 69-year-old man with a history of uric acid nephropathy was referred to our hospital with a complaint of hematemesis. No abdominal pain was revealed on physical examination. The laboratory data revealed that the eGFR was low at 22.1 mL/min/1.73 m^2 (Table 1, case 3). Carcinoembryonic antigen was 1.9 μg/L and carbohydrate antigen 19-9 (CA19-9) was 6.5 U/mL. Esophagogastroduodenoscopy revealed the presence of advanced (Borrmann type II) esophagogastric junctional cancer (Fig. 3A, B). CECT was performed using a dual-layer spectral detector with a reduction in contrast media of 30% of the conventional dose (iodine concentration of 186 mg/kg with 24 mL of iopamiron-370) to assess the location of the lesion and the presence of lymph node metastasis and distant metastasis of the cancer. The location of the lesion and the presence of metastasis were unclear by nonenhanced CT (Fig. 3C, D). Although the location of the lesion was clear on 120-kVp images, contrast enhancement was insufficient to assess the presence of metastasis (Fig. 3E-G). However, virtual monochromatic images at 40 keV revealed the location of the lesion and no lymph node metastasis, but clinical distant metastasis (Fig. 3H-J). Furthermore, preoperative abdominal CT angiography could be obtained regardless of the use of a reduced iodine load of up to 30% of the conventional dose (Fig. 3K). Because the tumor center of this cancer was located within 2 cm of the esophagogastric junction, the final diagnosis was advanced esophagogastric junctional cancer (clinical stage IIB; T2,N0,M0) according to TMN Classification of Malignant Tumors 8th edition published in 2017 [8]. He underwent total gastrectomy plus Roux-en Y reconstruction. Pathological findings of a surgical specimen revealed a 30 × 20-mm, poorly differentiated adenocarcinoma with microscopic lymphoid metastasis (pathological stage IIIA; T2,N1,M0).

Discussion

CECT using iodinated contrast media is useful for diagnosis of gastrointestinal diseases, such as extravasation of gastrointestinal bleeding, ischemia of the gastrointestinal tract, staging of digestive cancers, and qualitative diagnosis of the suspected disease. However, CIN caused by intravenous administration of iodinated contrast medium for CECT is problematic for patients with kidney disease.

According to current guidelines [2,3], CIN is a type of acute kidney injury caused by administration of iodinated contrast media. CIN is diagnosed when renal function decreases after administration of contrast media once other causes are ruled out. The definition of CIN is an increase in serum creatinine by ≥0.5 mg/dL or ≥25% from baseline within 72 hours after administration of iodinated contrast media. Although CIN is usually reversible, some patients may require hemodialysis because of deteriorated renal function. If CIN occurs after contrast-enhanced CT, the vital prognosis of patients with kidney disease could worsen.

A previous report revealed that baseline eGFR is associated with the incidence of CIN after CECT. The incidence of CIN

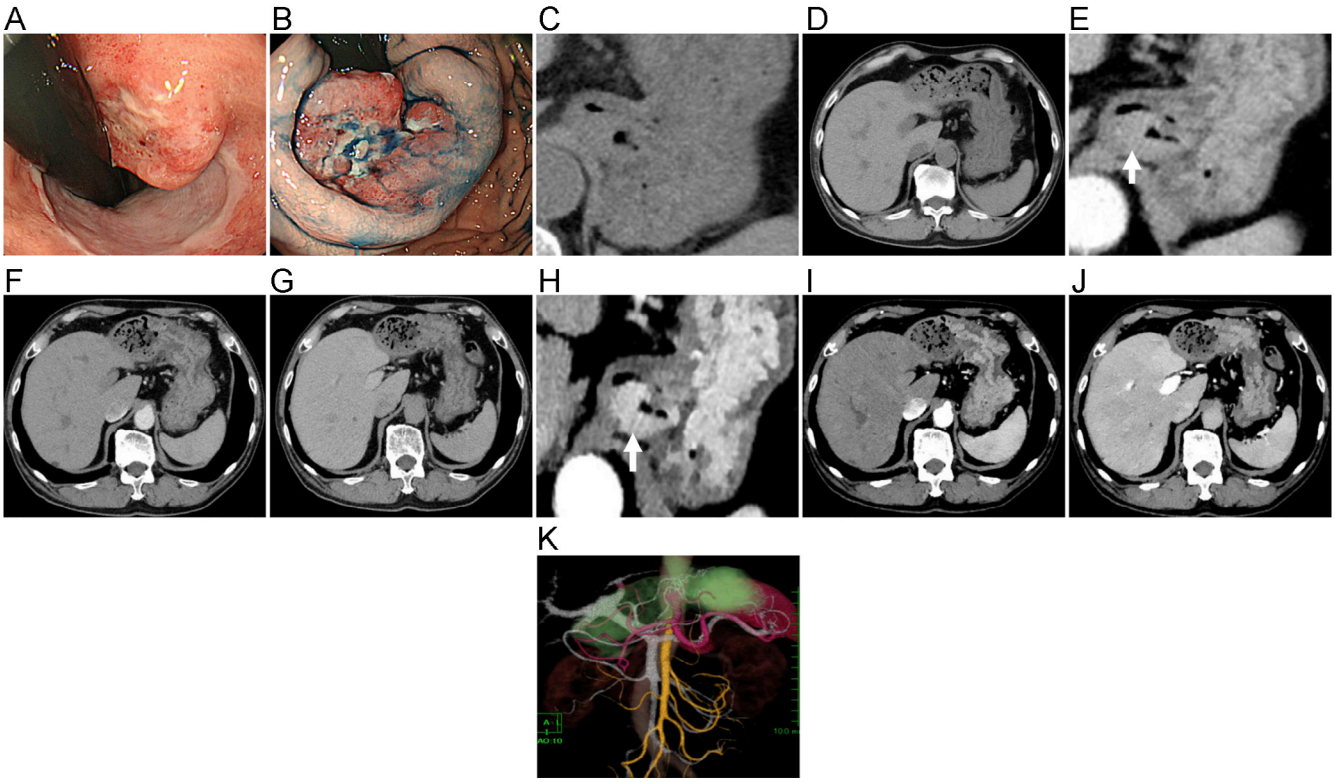

Fig. 3 – Contrast media of 30% of the conventional dose was used. (A,B) Esophagogastroduodenoscopy. The presence of advanced (Borrmann type II) esophagogastric junctional cancer was revealed. (C,D) Nonenhanced 120-kVp image. The location of the lesion and the presence of lymph node and distant metastasis was unclear. (E,F) Arterial phase of a 120-kVp image. (E) The location of the lesion was clear (white arrow). (F) Contrast enhancement was insufficient to assess the presence of lymph node and distant metastasis. (G) Portal phase of a 120-kVp image. Contrast enhancement was insufficient to assess the presence of lymph node and distant metastasis. (H,I) Aortal phase of a 40-keV image. The location of the lesion was clear. Contrast enhancement was sufficient to assess the presence of lymph node and distant metastasis. (J) Portal phase of a 40-keV image. Contrast enhancement was sufficient to assess the presence of lymph node and distant metastasis. (K) Abdominal CT angiography. Clear abdominal CT angiography before surgery could be obtained regardless of the use of reduced iodine load of up to 30% of the conventional dose.

among patients with a baseline eGFR of 45-59 mL/min/1.73 m^2 was 0%, whereas a rate of 30-44 mL/min/1.73 m^2 was 2.9% and <30 mL/min/1.73 m^2 was 12.1% [1]. According to available guidelines, a baseline eGFR of 45 mL/min/1.73 m^2 is a cutoff for the risk of CIN after intravenous administration of contrast media. Thus, prevention of CIN by hydration with normal saline or isotonic sodium bicarbonate and the use of minimal contrast media is recommended to reduce the risk of CIN [2,3].

Although the exact pathophysiology of CIN remains unclear, etiological factors include hypoxia in the renal medulla caused by endothelin secretion, reduced prostacyclin production [9], and cytotoxicity of contrast media of renal tissue, such as tubular cells [10,11]. Other than these pathophysiological characteristics, available guidelines state that the volume of contrast media is associated with the incidence of CIN. Therefore, the minimal use of contrast media to obtain adequate diagnostic information is recommended [2,3].

However, it is difficult to obtain adequate images with minimal contrast media by conventional CT, which provides only 120-kVp images corresponding to 70-keV images. On the other hand, dual-layer spectral detector CT enables the simultaneous collection of low- and high-energy data, and the imaging data acquired from dual-layer spectral detector CT can be reconstructed to virtual monochromatic images with photon energy levels of 40-200 keV by on-demand and immediate retrospective spectral analysis. Previous reports showed that CT attenuation and CNR had increased as the X-ray energy of virtual monochromatic images was decreased [6,12]. A past report revealed that 50-keV images achieved the same CNR of a 120-kVp image with a 2.5-fold reduction in iodine concentration and 40-keV virtual monochromatic images achieved the same CNR of a 120-kVp image with a 4.0-fold reduction in iodine concentration [6]. Thus, adequate images for diagnosis can be obtained by dual-layer spectral detector CT even if the amount of contrast media is reduced.

Dual-energy CT is an alternative strategy to acquire monoenergetic images [5]. However, there are some problems with dual-energy CT. First, because dual-energy CT irradiates low- and high-photon energy from the sides of independent dual X-ray tubes, spatial and temporal deviation between the dual-energy images may occur. Second, 120-kVp images, which are commonly obtained by conventional CT, cannot be obtained simultaneously. Third, use of a dedicated

protocol to set prescan settings is necessary before scanning. Therefore, clinicians must decide whether to perform dual-energy scanning before CT. Dual-layer spectral detector CT has overcome these downsides of dual-energy CT [13].

In case 1, extravasation of diverticular bleeding of the ascending colon was revealed by CECT on both 120-kVp and 50-keV images. Although hemostatic treatment was achieved endoscopically in this case, TAE would be necessary if endoscopic hemostatic treatment was not successful. It is important to locate the arterial bleeding source before preparation for TAE. The valuable point in this case was that the arterial bleeding source was clearly identified by abdominal CT angiography on 50-keV images even using a reduced amount of contrast media of 40% of the conventional dose. In case 2, it was important to determine whether the decreased blood perfusion in the transverse colon on 120-kVp and 50-keV images caused necrosis because prompt surgical intervention was necessary if the lesion was necrotic. Although hypo- or nonenhancement of the bowel wall is the most valuable finding of bowel ischemia, it is often difficult to confidently arrive at a diagnosis because these finding are often subtle [14,15]. However, a previous report showed that low-energy virtual monochromatic imaging and iodine-selective imaging were useful to identify subtle hypo- or nonenhancement of the bowel wall [16]. In this case, the transverse colon showed hypoenhancement in the arterial phase and improved enhancement in the portal phase. These findings were more conspicuous on 50-keV images than 120-kVp images because contrast enhancement of the nonischemic bowel was comparatively increased on the former. Furthermore, iodine-selective imaging was useful for diagnosis of severe hypoperfusion. CECT using 40% of the conventional dose of contrast media in dual-layer spectral CT was useful for diagnosis of severe hypoperfusion of the transverse colon with slight blood perfusion remaining. In case 3, staging of esophagogastric junctional cancer and abdominal CT angiography were performed before surgical resection regardless of the reduction in contrast media of up to 30% of the conventional dose. Although CECT is necessary to assess lymph node metastasis and distant metastasis in patients with digestive cancers, clinicians may hesitate to perform enhanced CT for patients with kidney disease, especially those with a baseline eGFR of <30 mL/min/1.73 m^2. This case showed that enhanced CT using a reduced amount of contrast media of up to 30% of the conventional dose in dual-layer spectral detector CT was sufficient to clinically assess the presence of lymph node metastasis and distant metastasis. Furthermore, it is beneficial to obtain clear images by CT angiography before surgery even with 30% of the conventional dose of contrast media.

Although CECT performed with a dual-layer spectral detector and reduced amount of contrast media offers the advantage of prompt and accurate diagnosis of various gastrointestinal diseases for patients with kidney disease, there are some limitations. First, the conspicuous texture of low-energy virtual monochromatic images is problematic. A previous report showed that monochromatic images at 70 keV have similar texture to conventional CT images acquired at 120 kVp and the texture becomes noticeable on 50-keV images [17]. Therefore, conspicuous image texture as shown in case 3 (Fig. 3H–J) may become a disadvantage for the interpretation of virtual monochromatic images at low-energy such as 50 or 40 keV. Second, there is no established evidence-based protocol to reduce the amount of contrast media.

In conclusion, low-energy virtual monochromatic images acquired with a dual-layer spectral detector and a reduced amount of contrast media is useful to diagnose various gastrointestinal diseases for patients with kidney disease and a baseline eGFR of <45 mL/min/1.73 m^2. The texture of virtual monochromatic images at low energy and the absence of an evidence-based protocol to reduce the amount of contrast media are limitations of dual-layer spectral detector CT at this time.

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