Spectral Photon-counting CT: Initial Experience with Dual–Contrast Agent K-Edge Colonography[1]

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Purpose: To investigate the feasibility of using spectral photon-counting computed tomography (CT) to differentiate between gadolinium-based and nonionic iodine-based contrast material in a colon phantom by using the characteristic k edge of gadolinium.

Materials and Methods: A custom-made colon phantom was filled with nonionic iodine-based contrast material, and a gadolinium-filled capsule representing a contrast material–enhanced polyp was positioned on the colon wall. The colon phantom was scanned with a preclinical spectral photon-counting CT system to obtain spectral and conventional data. By fully using the multibin spectral information, material decomposition was performed to generate iodine and gadolinium maps. Quantitative measurements were performed within the lumen and polyp to quantitatively determine the absolute content of iodine and gadolinium.

Results: In a conventional CT section, absorption values of both contrast agents were similar at approximately 110 HU. Contrast material maps clearly differentiated the distributions, with gadolinium solely in the polyp and iodine in the lumen of the colon. Quantitative measurements of contrast material concentrations in the colon and polyp matched well with those of actual prepared mixtures.

Conclusion: Dual-contrast spectral photon-counting CT colonography with iodine-filled lumen and gadolinium-tagged polyps may enable ready differentiation between polyps and tagged fecal material.

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Colorectal cancer is the third leading cause of cancer-related death worldwide (1). For 2015, the American Cancer Society estimated that about 49700 deaths due to colorectal cancer will have occurred (2). Because most colorectal cancers develop from precancerous polyps, early detection and treatment of colonic polyps make up a major goal in the fight against cancer. Screening for colorectal cancer is usually performed with colonoscopy, which has been reported to reduce colorectal cancer–related mortality by up to 30% (3,4).

Computed tomographic (CT) colonography is an alternative method for noninvasive evaluation of the colon and is also recommended by the American Cancer Society as a screening option (5). Other investigations have shown that the diagnostic performance of CT colonography for the detection of colon polyps is similar to that of conventional colonoscopy (6,7). However, both methods, conventional as well as CT-based colonography, require a cathartic preparation of the bowel; the bowel preparation lowers patient adherence and acceptance of the procedure, especially as a screening method (8). This is particularly true for elderly patients and those with multiple morbidities.

A new approach for CT colonography that does not entail cathartic cleansing of the bowel, so-called laxative-free colonography, uses barium or iodine for tagging of the feces (8,9). In combination with an appropriate diet adjustment, oral ingestion of a water-soluble iodinated contrast agent enables contrast enhancement of the fecal material and residual fluid in the bowel. When the CT examination is finished, a software application virtually removes the contrast agent–enhanced fecal material from the images (so-called electronic cleansing) (10,11). Although this novel CT colonographic method may increase patient acceptance of the procedure, it has technical limitations, including reduced diagnostic image quality and limited differentiation owing to unclear tagging. These limitations cause small polyps and flat lesions to be missed and thus a reduction in sensitivity and specificity (12).

The introduction of spectral photon-counting CT in the clinical arena may overcome most limitations associated with laxative-free colonography. With respect to diagnostic image quality, an improvement of spatial resolution, improved signal-to-noise ratio, and reduction of beam-hardening artifacts can be expected. Initial pilot studies have demonstrated the possibility of using spectral photon-counting CT data for diagnostic tasks (13). Furthermore, the ability of spectral photon-counting CT to exploit the characteristic k edges of contrast agents substantially improves the differentiation between enhanced polyps and remaining stool in the colon.

The important advantages of a spectral photon-counting CT system, compared with current CT technology, are based on the concept that incoming photons are counted and spectrally binned by analyzing the pulse heights generated in a semiconductor detection layer (14–16). Recent developments showed promising results with regard to high flux rates for room-temperature semiconductor photon-counting detectors (17). These developments not only present an incremental technical advancement but also result in a paradigm shift in the clinical routine because spectral photon-counting CT now enables the radiologist to differentiate between two contrast agents in a single CT acquisition. In the case of CT colonography, for example, one contrast agent could be administered intravenously for enhancement of polyps and a second contrast agent could be administered orally for tagging of the fecal material and residual fluid in the bowel. In this study, we investigated the feasibility of using spectral photon-counting CT to differentiate between gadolinium- and nonionic iodine-based contrast material in a colon phantom by using the characteristic k edge of gadolinium.

Advances in Knowledge

- This study demonstrates the feasibility of spectral photon-counting CT for laxative-free colonography.
- Contrast material maps derived from spectral photon-counting CT of the simulated colon clearly differentiated the distributions of gadolinium solely in the simulated polyp and of iodine in the lumen.
- Quantitative measurements of contrast material concentrations in the phantom lumen and the simulated polyp matched well with those in actual prepared mixtures.

Implication for Patient Care

- Laxative-free colonography with spectral photon-counting CT may provide improved results compared with conventional CT colonography because it can be reliably used to differentiate gadolinium-enhanced polyps and iodine-tagged fluids and feces.

Materials and Methods

E.R., I.B., M.B., P.C., H.D., B.B., A.T., M.R., and R.P. are employees of Philips Healthcare. The remaining authors (D.M., D.B.N., A.A.F., S.R., F.K.K., J.H., L.B., F.P., E.J.R, P.D., and P.B.N.) have no financial conflicts of interest and had complete, unrestricted access to the study data at all stages of the study.

Colon Phantom

Commercially available CT phantoms do not have the material characteristics necessary for experiments with spectral photon-counting CT systems because they may include other k-edge

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Conflicts of interest are listed at the end of this article.

Figure 1

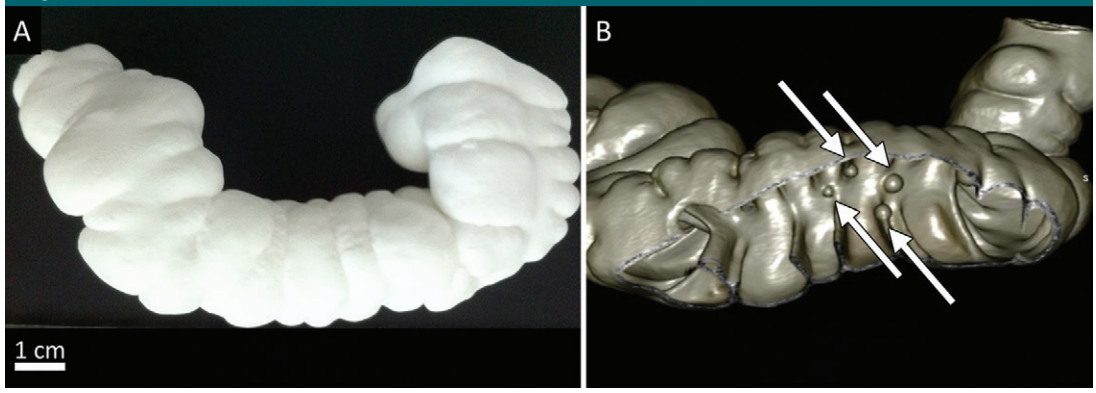

Figure 1: Colon phantom. *A*, Photograph of colon phantom. Apart from minor fabrication deviations, phantom represents digital model. *B*, Three-dimensional volume rendering of phantom generated from CT data acquired with conventional scanner. Polyps, which were added to phantom before production, can be seen inside colon (arrows).

materials, which can compromise spectral results. We therefore used a rapid-prototyping method to fabricate a custom-made phantom by using an additive manufacturing technique of selective laser sintering based on polyamide 12. To mimic the real case, the complex geometry and structure of a colon were segmented from a routinely acquired CT scan. This digital model of the colon was then modified by inserting nonenhancing polyps. To match the mass attenuation coefficient of the colon wall, a mixture of the polymer structure based on polyamide 12 and additional filler material (low-Z material without k edges in the relevant energy range) was calibrated with a conventional CT system. Finally, the customized CT colon phantom was three-dimensionally printed with selective laser sintering (Fig 1). In addition, a gadolinium-filled capsule representing an enhanced polyp was positioned on the colon wall.

Spectral Photon-counting CT

The multibin preclinical spectral photon-counting CT system (Philips Healthcare, Haifa, Israel) is based on a semiconductor detector technology operated in single photon-counting mode with energy discrimination (18,19). The in-plane field of view was 168 mm, with a z-coverage in the scanner isocenter of 2.5 mm. Axial scans over 360° were obtained with a tube current of 50 mA, a tube voltage of 120 kVp, a scanner rotation time of 1 second, and 2400 projections per rotation. The noise threshold was set to 30 keV; for optimal discrimination between iodine and gadolinium, a second threshold was set to the k-edge energy of gadolinium.

The custom-made colon phantom consisted of a main body (representing the colon) and a contrast-enhanced capsule (representing the enhanced polyp) attached to the colon wall. The main body of the colon was filled with a nonionic iodine-based contrast agent (Bracco, Milan, Italy), and the polyp was filled with gadolinium (Bayer Pharma, Berlin, Germany). For each contrast agent, the concentrations are chosen such that, in a conventional CT section, the Hounsfield unit measures were similar, with approximately 110 HU (Fig 2): 0.021 mmol/mL iodine and 0.012 mmol/mL gadolinium.

Material Decomposition and Quantitative Measurements

Multibin photon-counting data were preprocessed, and a conventional CT image was derived from the information contained in all energy bins. In addition, after pileup correction, the multibin counting data were used to trigger a maximum likelihood–based material decomposition of the attenuation into a water, iodine, and gadolinium material basis (14,15). Conventional filtered back-projection reconstructions were used without further postprocessing apart from deringing, as well as smoothing of the gadolinium k-edge image with a Gaussian kernel 1 mm wide. The gadolinium overlay used in Figure 3, *D*, was smoothed by a 3-mm Gaussian kernel. All images were reconstructed on a voxel grid of 0.39 × 0.39 × 0.25 mm. The iodine and gadolinium images were averaged to a section thickness of 1 mm.

Results

A conventional CT image of the colon phantom with differently sized polyps is shown in Figure 2, *A*. Present in this section are the main body of the colon filled with nonionic iodine (*i* in Fig 2, *A*), the polyp filled with gadolinium (*ii* in Fig 2, *A*), and a nonenhanced polyp (*iii* in Fig 2, *A*). The quantitative measurements of iodine (mean ± standard deviation, 113 HU ± 3) and gadolinium (108 HU ± 4) reveal similar Hounsfield units for both materials. Figure 2, *B*, shows a profile along a gradient (red to blue) line in the conventional CT image. This figure shows that both materials have similar Hounsfield units.

Figure 3 depicts spectral photon-counting CT of the colon phantom. The different panels show the conventional CT image (Fig 3, *A*), the conventional CT image with an overlay of iodine (green) and gadolinium (pink) (Fig 3, *B*), an iodine map (Fig 3, *C*), and a gadolinium map (Fig 3, *D*). Both material images (Fig 3, *C* and *D*) are generated from

Figure 2

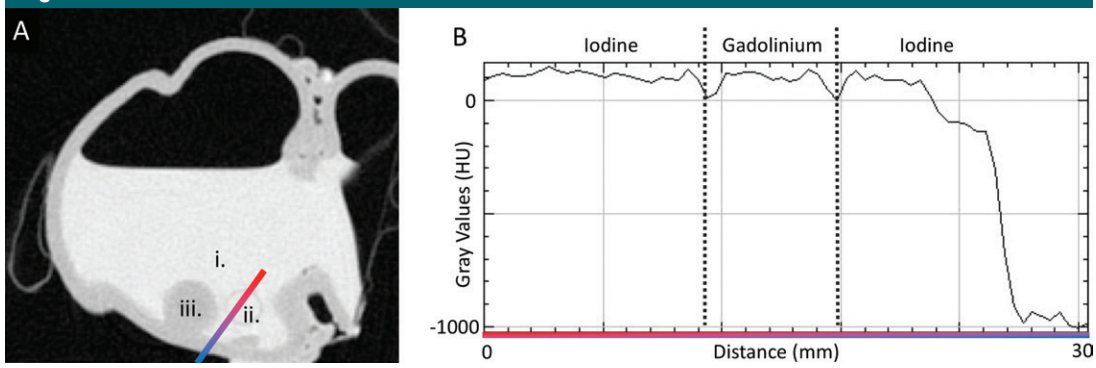

Figure 2: *A*, Conventional CT scan generated from photon-counting image shows main body of colon filled with nonionic iodine *(i)*, polyp filled with gadolinium *(ii)*, and nonenhanced polyp part of phantom *(iii)*. *B*, Profile along gradient (red to blue) line quantitatively demonstrates that both materials have a similar Hounsfield unit.

the decomposition algorithm and are visually and quantitatively clearly distinguishable. Therefore, this procedure enables a separation between gadolinium-enhanced polyp tissue and iodine-tagged feces and fluids in the colon.

Furthermore, spectral photon-counting CT enables quantitative measurement of contrast agent concentrations. In the iodine-filled colon, the iodine concentration was 0.02 mmol/mL ± 0.01 and the gadolinium concentration was 0.00 mmol/mL ± 0.003. In the gadolinium-filled polyp, the iodine concentration was 0.00 mmol/mL ± 0.01 and the gadolinium concentration was 0.011 mmol/mL ± 0.004. As a reference, the original concentrations of iodine and gadolinium were 0.021 mmol/mL and 0.012 mmol/mL, respectively.

Discussion

In this study, we demonstrated that spectral photon-counting CT enabled discrimination of iodine-filled lumen and gadolinium-enhanced polyp in an experimental colon phantom. The differentiation among small and/or flat polyps, contrast material in the colon, and contrast-enhanced fecal material is a major challenge in laxative-free CT colonography with electronic cleansing. Usually, oral ingestion of a positive contrast agent (eg, iodine) is used to tag the fecal material and the residual fluid in the colon (8,9,20). After CT, a postprocessing algorithm (electronic cleansing) removes the fecal material, which is tagged by iodine, from the CT data set. For a reliable electronic cleansing procedure, however, it is essential to remove all the fecal material but to preserve polyps, colonic tissue, or tumors in the CT images (20). Therefore, accurate differentiation between the different materials and tissue is mandatory.

In conventional single-energy CT colonography, the differentiation between fecal residue and polyps is based solely on the absorption values of the different materials. Therefore, optimal colonic preparation and distention are essential for a viable diagnostic assessment of the colon (21). However, colonic preparation is suboptimal in up to 66% of patients (22). In addition, several artifacts typically occur in single-energy CT colonography, such as beam-hardening pseudo-enhancement caused by incomplete cleansing of folds and polyps adjacent to contrast material–tagged fecal materials, partial volume effects, and inhomogeneous tagging with incomplete cleansing (23). Improvements can be obtained with dual-energy CT, but this technology does not overcome all challenges of laxative-free colonography. Rapid kilovolt peak switching (24), dual-layer detectors (25), and dual x-ray sources (26) are technical features that allow assessment of CT values of an object scanned with two different effective x-ray spectra (27). The comparison of CT values assessed at higher and lower kilovolt peak settings provides additional information on the tissue or material, depending on its effective atomic number. This helps improve the differentiation between two materials, such as soft tissue from the tagged fecal material (11). Furthermore, previous research showed that image quality can be improved (eg, reduced beam hardening and improved iodine signal) with virtual monochromatic approaches (28). However, dual-energy approaches offer only limited material decomposition and consequently cannot help easily differentiate between two contrast agents (eg, iodine and gadolinium embedded in the soft-tissue matrix).

The limitations of our study include the use of gadolinium as a CT contrast material. Gadolinium is not a standard contrast agent in routine CT imaging. The concentration of the gadolinium was chosen because of the iodine enhancement of the fecal materials in the colon. Thus, the gadolinium concentration was matched to achieve similar Hounsfield units. Therefore, we could demonstrate the potential of material separation even at identical Hounsfield units. With respect to instructions made by the pharmaceutical industry, the expected concentration of intravenously injected gadolinium was 1.5 to two times greater than the current maximum dose recommended for clinical practice. Additional limitations of our study are the use of a limited field of view and the absence of any in vivo data. In the future it will be necessary to translate our results to a clinically relevant field of view in an in vivo model.

In summary, the results of our study of a preclinical spectral photon-counting

Figure 3

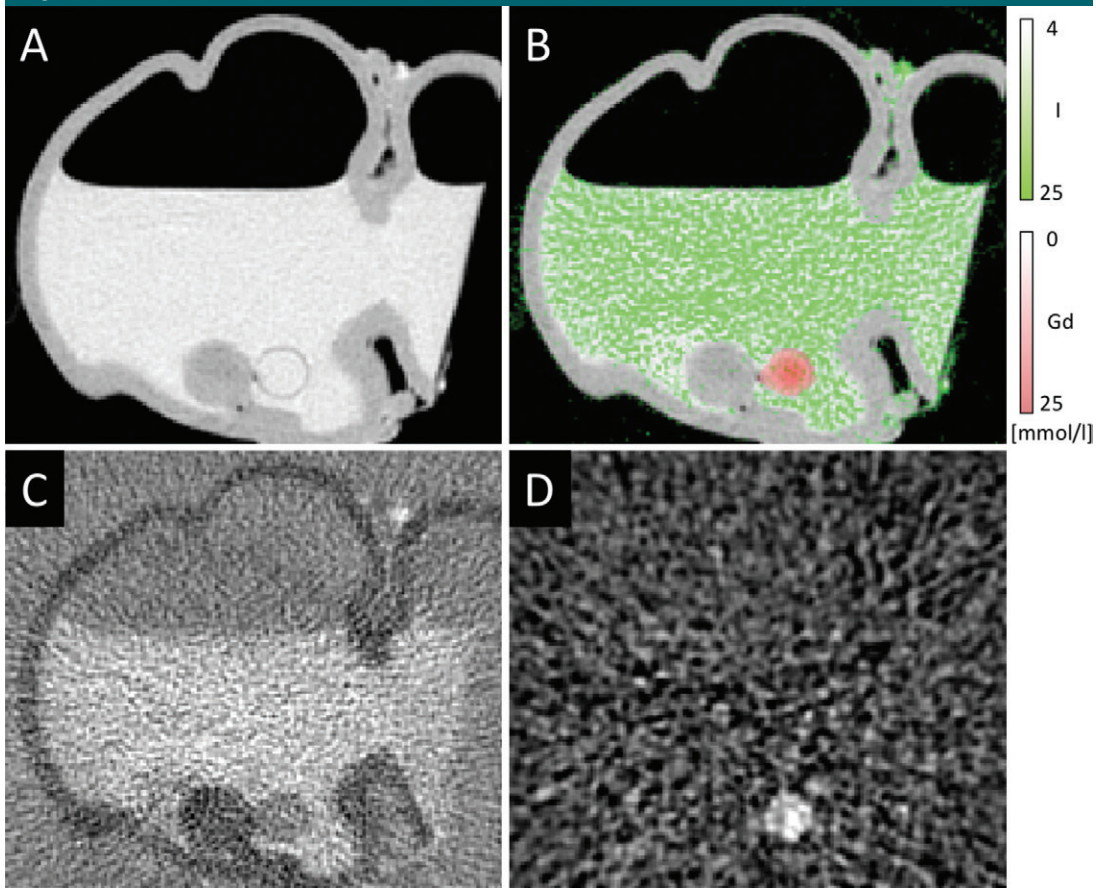

Figure 3: Photon-counting CT of colon phantom. *A*, Conventional CT scan (window: −300 HU, level: 1000 HU). *B*, Conventional CT scan (image in *A*) with overlay of iodine (green) and gadolinium (red). *C*, Iodine image (window: 0 mmol/L, level: 80 mmol/L). *D*, Gadolinium image (window: 5 mmol/L, level: 20 mmol/L). Both material images (*C* and *D*) are generated from decomposition algorithm and are visually and quantitatively distinguishable. Therefore, this procedure enables a separation between gadolinium-enhanced polyp tissue and iodine-tagged fluids and feces in colon.

CT system illustrate that precise material decomposition with separation of iodine and gadolinium is feasible in a colon phantom. With use of the spectral information from spectral photon-counting CT, separate iodine and gadolinium images were calculated, illustrating the distribution of both materials. In addition, quantitative measurements of gadolinium and iodine are possible.

In this study, we propose a spectral photon-counting CT colonographic examination protocol, including intravenous contrast material application (gadolinium) for enhancement of the polyp and oral ingestion of iodine for fecal tagging. The electronic cleansing would thus be inherently done by the combination of spectral photon-counting CT scan acquisition and material decomposition. On the basis of the potential of this material-specific imaging, the gadolinium-enhanced polyp tissue and the iodine-tagged fluid and feces in the colon can be reliably differentiated. Thus, this system can ensure preservation of polyps, colonic tissue, or tumors on the CT images. In the future, large evaluation studies with clinical spectral photon-counting CT systems will be necessary to prove the clinical benefit of the proposed spectral photon-counting CT colonographic protocol.

In conclusion, we reported on the experimental spectral photon-counting CT colonographic results from a preclinical spectral photon-counting CT system. This system shows the possible clinical path toward full use of spectral photon-counting CT systems; the clinical introduction of such a system may provide improved diagnostic imaging.

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