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FULL PAPER

Submillisievert chest dual energy computed tomography: a pilot study

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Objective: To assess if diagnostic dual energy CT (DECT) of the chest can be achieved at submillisievert (sub-mSv) doses.

Methods: Our IRB-approved prospective study included 20 patients who were scanned on dual-source multidetector CT (MDCT). All patients gave written informed consent for acquisition of additional image series at reduced radiation dose on a dual-source MDCT (80/140 kV) within 10 s after the standard of care acquisition. Dose reduction was achieved by reducing the quality reference milliampere-second, with combined angular exposure control. Four readers, blinded to all clinical data, evaluated the image sets. Image noise, signal-to-noise and contrast-to-noise ratio were assessed. Volumetric CT dose index (CTDI_{vol}), dose-length product (DLP), size specific dose estimate, and effective dose were also recorded.

Results: The mean age and body mass index of the patients were $71 \text{ years} \pm 9$ and $24 \text{ kg m}^{-2} \pm 3$, respectively. Although images became noisier, overall image

quality and image sharpness on blended images were considered good or excellent in all cases (20/20). All findings made on the reduced dose images presented with good demarcation. The intraobserver and interobserver agreements were $\kappa = 0.83$ and 0.73 , respectively. Mean CTDI_{vol} , size specific dose estimate, DLP and effective dose for reduced dose DECT were: $1.3 \pm 0.2 \text{ mGy}$, $1.8 \pm 0.2 \text{ mGy}$, $51 \pm 9.9 \text{ mGy.cm}$ and $0.7 \pm 0.1 \text{ mSv}$, respectively.

Conclusion: Routine chest DECT can be performed at sub-mSv doses with good image quality and without loss of relevant diagnostic information.

Advances in knowledge: (1) Contrast-enhanced DECT of the chest can be performed at sub-mSv doses, down to mean CTDI_{vol} 1.3 mGy and DLP 51 mGy.cm in patients with body mass index $<31 \text{ kg m}^{-2}$. (2) To our knowledge, this is the first time that sub-mSv doses have been successfully applied in a patient study using a dual source DECT scanner.

INTRODUCTION

CT has been recognized as an important source of radiation exposure to the general population.¹ This finding has led to efforts to reduce CT radiation dose levels to those “as low as reasonably achievable”.² Although dose reduction is desirable, diagnostic information must not be compromised. Advances in CT technology, including iterative reconstruction algorithms and tube current modulation, have yielded diagnostic low dose CT imaging of multiple body segments.^{3,4} In the domain of thoracic imaging, ultra low dose protocols have been successfully implemented in several clinical scenarios, including lung cancer screening.^{5,6}

When dual energy CT (DECT) was first approved for clinical use, it was associated with higher radiation dose levels than single energy CT.⁷ Since DECT’s introduction,

however, the same technical advances used for single energy CT scanners have been successfully applied to DECT scanners to reduce the radiation associated with the operation of the X-ray tubes at low and high tube potential (kVp) and to reduce the image noise associated with low radiation dose protocols.⁸ The lowest dose capable to achieve a diagnostic DECT is unknown. To our knowledge, ultra low dose protocols for chest DECT have not yet been tested in patient studies.

The purpose of our study is to assess if diagnostic DECT of the chest can be achieved at submillisievert (sub-mSv) doses, without loss of diagnostic information.

METHODS AND MATERIALS

The Human Research Committee of our Institutional Review Board approved this prospective study. Written

informed consent was obtained from all participants. The study was conducted in accordance with the Health Insurance Portability and Accountability Act guidelines for research. Our radiology department received a research grant from Siemens Healthcare. All authors had complete unrestricted access to the data.

Patients

In order to identify patients scheduled for a contrast-enhanced routine chest CT, one study co-investigator (RC) reviewed the Radiology Information System. The patients were then assessed for inclusion and exclusion criteria. Inclusion in the study required that patients be conscious, oriented, able to provide written consent, aged ≥ 56 years old and haemodynamically stable. Patients were excluded if they were undergoing emergency CT, were unable to hold their breath for 10 s or more, had a history of allergic reaction to contrast media and/or had a body mass index (BMI) $\geq 32 \text{ kg m}^{-2}$.

After this initial assessment, the same co-investigator explained the study details, procedures and associated risks for all patients. 31 patients declined taking part in the study. 23 patients of the initial 54 deemed eligible accepted participation in the study and were approached by a second co-investigator who completed the consent process and answered additional questions. Three patients withdrew from the study after signing the informed consent because they were unwilling to wait and undergo chest CT in the DECT scanner (instead, undergoing CT in a different scanner). A flow chart showing subject enrollment is provided in Figure 1.

20 adult patients formed our final cohort (9 males and 11 females; mean age 71 ± 9 years (range from 56 to 88 years), with mean age for males, 77 ± 8 years and for females, 67 ± 6 years) (Table 1). All patients were scheduled for standard of care contrast-enhanced chest CT for different clinical indications including

Table 1. Characteristics of patients included in our study

Characteristics	Male	Female
Number of patients	9	11
Age (mean + SD) in years	77 ± 8	67 ± 6
Weight (kg)	70 ± 9	64 ± 12
BMI (mean + SD) in kg m^{-2}	24 ± 2	23 ± 5
Number of patients with different BMI		
$\leq 20 \text{ kg m}^{-2}$	0	1
$20.1\text{--}25 \text{ kg m}^{-2}$	7	5
$25.1\text{--}30 \text{ kg m}^{-2}$	2	3
$30.1\text{--}32 \text{ kg m}^{-2}$	1	0

BMI, body mass index, SD, standard deviation.

neoplasm surveillance, persistent cough and/or staging for extrathoracic malignancies.

Scanning techniques

All chest CT examinations included in our study were performed on a 64-row, dual-source, MDCT scanner (Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany), with flying focal spot (double z-sampling). All CT examinations were performed using 80 ml of intravenous iodinated contrast medium (Iopamidol 370, Bracco Diagnostics, Princeton, NJ). The contrast was injected at a rate of 2.5 ml s^{-1} , with a fixed delay (57 s) as a trigger to scan the patient. The acquisition duration for each scan series was identical (around 3 s). Both standard of care and ultra low-dose dual energy series (research images) covered the lung apices down through the upper pole of the kidneys. The ultra low-dose image series was acquired within 10 s after the standard of care CT image series. For the research images, the quality reference milliamperes-second (mAs) (CARE Dose 4D, Siemens Healthcare, Forchheim, Germany) was reduced to achieve $\approx 25\%$ of the radiation dose delivered by the standard of care dose protocol.⁹ All other acquisitions parameters were kept constant and no additional intravenous contrast was administered beyond that required for the initial clinically warranted examination. The scan parameters are summarized in Table 2.

The volumetric CT dose index (CTDI_{vol}) and dose-length product (DLP) for each image series were recorded. In addition, we recorded water equivalent diameter (D_w) for each patient from radiation dose tracking and monitoring software (Radiometrics Enterprise Platform, Bayer Inc., Whippany, NJ). The size specific dose estimate (SSDE) was calculated by multiplying D_w by a conversion factor provided by the American Association of Physicists in Medicine.¹⁰ Effective dose (ED) for all chest CT examinations were calculated by multiplying the DLP by a conversion coefficient for chest CT (0.014).¹¹

Image reconstruction

All images were reconstructed using sinogram-affirmed iterative reconstruction (SAFIRE, Siemens Healthcare, Forchheim, Germany) at noise reduction strength of Level 3 (S3) settings and a standard of care soft-tissue reconstruction kernel

Figure 1. Flowchart of cohort formation. sub-mSv, submillisievert.

Table 2. Scan parameters for standard of care and reduced dose dual energy CT

	Standard of care	Reduced dose
Voltage tube A (kV)	80	80
Voltage tube B (kV)	140 (with tin filter)	140 (with tin filter)
Quality Reference mAs	180	45
Acquisition (mm)	128 × 0.6	128 × 0.6
Rotation time (s)	0.5	0.5
Pitch	1.2	1.2
Direction	Craniocaudal	Craniocaudal
Slice thickness (mm)	3	3
Slice increment (mm)	2	2
Kernel	I30f and I50f	I30f and I50f
Window	Mediastinum	Mediastinum
Safire	3	3

(I30f Med Smooth). Blended images (80/Sn140 kV) were reconstructed in transverse orientation at a section thickness of 3 mm and an increment of 2 mm, using a standard of care hard reconstruction kernel (I50f) in order to evaluate the lung parenchyma. Virtual monochromatic images at 40 and 60 keV (standard of care and ultra low-dose series) were generated using image-processing software (Syngovia, Siemens Healthcare, Forchheim, Germany). We chose to use these images for analysis, in addition to blended images, because they have similar or less noise compared with blended images and can enhance the conspicuity of iodine.^{12–15} The 40 keV images were selected because they are closest to the k-edge of iodine (33 keV). The 60 keV images were selected because they have less noise than 40–50 keV images but have superior contrast compared with previously reported 65–70 keV images for evaluation of mediastinum and lung parenchyma.^{16,17} All scan parameters and patient information were de-identified prior to subjective evaluation of the images.

Subjective assessment

Four board-certified, subspecialty trained thoracic radiologists (JA, AS, SM, and MP, with 21, 19, 10 and 7 years of experience, respectively) assessed chest CT images independently on a Digital Imaging and Communications in Medicine compliant image viewer—ClearCanvas (ClearCanvas Inc., Toronto, Canada). All readers were blinded to the identity of each image series.

The first two readers (JA and AS) performed the lesion detection assessment on blended images (using both I30f and I50f kernels), separated in 2 image sets. Set 1 (20 images) contained a mix of full and reduced radiation dose images in random order. Set 2 (20 images) contained the complementary pair of images to Set 1. As an example, if the ultra low-dose image of one patient was assessed on the Set 1, the standard of care image of the same patient would be assessed on Set 2. In order to eliminate any recall bias, the Set 2 images were assessed 3 weeks after the Set 1 images.

The other two readers (SM and MP) performed a side-by-side comparison between imaging findings on 60 keV virtual monochromatic standard of care and reduced dose images (using I30f kernel). A side-by-side approach was deemed suitable because this was a proof-of-concept study to assess whether the image quality on monochromatic images was comparable for both protocols and whether the increase in noise could compromise the lesion assessment on post-processed images.

The readers evaluated mediastinal and/or parenchymal lung lesions and anatomic structures (such as pulmonary nodules, lung fissures, subsegmental bronchial walls, pericardium and subcentimetre mediastinal lymph nodes) on blended and virtual monochromatic images at 60 keV for overall image quality using a 5-point scale (1—lesions and structures not seen; 2—lesions and structures barely visible with unreliable interpretation; 3—lesions and structures visible, with a blurring and uncertainties about the evaluation; 4—lesions and structures visible with blurring but without restriction of diagnosis; 5—lesions and structures clearly visible with good demarcation). Image sharpness was also evaluated on blended images using a 5-point scale (1—non-diagnostic; 2—noticeable blur, poorly defined edges; 3—moderately unsharp, questionable diagnostic difference; 4—mildly unsharp edges, no diagnostic difference; 5—very sharp).

Objective assessment

Image noise (defined as the standard deviation of the voxel values) and signal (CT numbers, Hounsfield units—HU) were obtained by placing three regions of interest (ROIs) in the air of the tracheal lumen right above carina, in a vertebral body (T12) and in the left paraspinal muscle at the same level. CT numbers in the left pulmonary artery were also measured. The ROIs (0.5–0.8 mm² in area) were drawn by a single investigator (RC) on blended and virtual monochromatic images at 60 and 40 keV from both standard of care and reduced dose datasets.

The contrast-to-noise ratio (CNR) and signal-to-noise ratio (SNR) were also calculated. The ROI of the trachea was used as a reference for calculation of the CNR.¹⁸

Given the 10 s delay between the standard of care and research image series, quantitative measurements of iodine concentration were not performed.

Statistical analysis

The data were analysed using SPSS for Mac (v. 24.0. IBM Corp., Armonk, NY). A Student's *t*-test was used to compare image noise and attenuation in the right pulmonary artery between both groups. The Wilcoxon paired signed-rank test was used to assess differences between subjective image quality characteristics on standard of care and reduced dose DECT image series. Inter-observer agreement in terms of subjective variability was measured with Cohen κ statistics. A $\kappa \leq 0.20$ was regarded as poor, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 good, 0.81–0.99 excellent and 1 perfect. A *p*-value <0.05 was considered statistically significant.

RESULTS

The demographics of the patient cohort are summarized in Table 1.

Subjective assessment

Visualization of normal pulmonary structures (lung fissures and subsegmental bronchi wall), subcentimetre lymph nodes (para-tracheal, subcarinal and hilar), and pericardium were identical on standard of care and reduced dose DECT images for both blended and 60 keV virtual monochromatic images.

Lesion assessment performance on blended images

Abnormalities detected on the DECT images included non-calcified subcentimetre solid pulmonary nodules, ranging in size from 2 to 10 mm ($n = 19$); pulmonary non-calcified solid nodules >10 mm ($n = 2$); emphysema ($n = 5$); superior vena cava syndrome ($n = 1$); ground glass nodules ($n = 3$); postsurgical changes ($n = 5$); mediastinal and hilar lymphadenopathy ($n = 1$); aortic valve replacement ($n = 1$); pleural effusion ($n = 3$); tree-in-bud pattern ($n = 2$); pericardial effusion ($n = 1$); and bronchiectasis ($n = 1$).

All mediastinal lesions were detected on the ultra low dose DECT images by the first two readers with perfect inter-observer agreement ($\kappa = 1$). The images were considered very sharp (5 points); lesions and structures were clearly visible with good demarcation (5 points).

Regarding the pulmonary parenchymal findings, the ultra low-dose protocol allowed detection of pulmonary nodules as small as 2 mm (Figures 2 and 3). The reported intraobserver agreement was excellent for Reader 1 ($\kappa = 0.83$) and good for

Figure 3. Contrast-enhanced DECT in a 69-year-old-female (BMI 18.8 kg m⁻²) for hemoptysis. (a) Blended images and (b) monochromatic images at 60 keV from standard of care DECT show cystic bronchiectasis and patchy nodular and ground glass opacities in the right upper lobe. (c) Blended and (d) monochromatic images at 60 keV from ultra low-dose DECT demonstrated the same findings. Overall image quality was considered excellent by the readers.

Figure 2. Contrast-enhanced DECT in a 70-year-old-male (BMI 25.9 kg m⁻²) for nodule follow-up. (a) Blended images, (b) monochromatic images at 60 keV and (c) at 40 keV (standard of care dual energy CT) show an indeterminate small nodule (arrow) in the left lower lobe. (d) Blended images, (e) monochromatic images at 60 keV and (f) at 40 keV (reduced dose DECT) demonstrate the same nodule. Overall image quality was considered excellent by the readers. BMI, body mass index; DECT, dual energy CT.

reader 2 ($\kappa = 0.78$). The inter-observer agreement was considered good ($\kappa = 0.66$ for Set 1 images and $\kappa = 0.73$ for Set 2 images). The overall image quality was considered excellent (5 points) by both readers in all ultra low-dose images (lung and mediastinal windows). Image sharpness was considered excellent in 19/20 cases and good in 1/20 case (but still diagnostic). One of the readers found it challenging to detect extremely mild centrilobular emphysema on the ultra low-dose image series. There was no difficulty detecting moderate or severe emphysema.

Side-by-side comparison on monochromatic images

All parenchymal and mediastinal lesions detected on 60 keV virtual monochromatic images (standard of care protocol) were also seen on the virtual monochromatic images using the ultra low dose DECT protocol and vice-versa. The overall image quality achieved the highest score on the 5-point scale for all the cases. No significant difference in lesion conspicuity was detected between the images series.

Per our standard of care clinical practice, only one kernel (I30f) is used for reconstructing monochromatic images. Therefore, image sharpness was not evaluated. For the same reason, a

Table 3. Objective assessment of image noise, SNR and CNR on blended images for standard of care chest DECT and reduced dose chest DECT

	Standard of care DECT	Reduced dose DECT	% difference
Blended images			
Image noise			
Trachea	10.0 ± 1.3	12.2 ± 4.0	22%
Muscle	14.9 ± 4.4	20.6 ± 4.4	38%
Bone	28.9 ± 8.3	34.8 ± 7.6	20%
SNR			
Trachea	101.1 ± 12.7	85.9 ± 19.3	-15%
Muscle	4.0 ± 1.4	2.8 ± 1.3	-30%
Bone	4.5 ± 1.5	4.1 ± 1.6	-9%
CNR			
Muscle	95.6 ± 12.1	81.2 ± 18.0	-15%
Bone	88.1 ± 10.9	74 ± 17.0	-16%

CNR, contrast-to-noise ratio; DECT, dual energy CT; SNR, signal-to-noise ratio.

Note: Numbers represent mean image noise, mean SNR and mean contrast-to-noise ratio and standard deviation of the mean.

comparison between blended and monochromatic images did not seem suitable.

Objective assessment

Mean HU values in the left pulmonary artery were 173 ± 15 and 217 ± 73 HU for ultra low dose blended and 60 keV monochromatic images, respectively; and 312 ± 14 and 402 ± 36 HU for standard of care blended and 60 keV monochromatic images,

respectively. The mean HU value in the left pulmonary artery on 40 keV monochromatic images (ultra low dose protocol) was 6% higher (mean 428 ± 85 HU) than the mean HU value of the left pulmonary artery on the 60 keV monochromatic images (standard of care protocol), despite the 10 s delay between both protocols.

Tables 3 and 4 show the results of the objective image quality study. An increase in noise and a decrease in SNR and CNR were found for all ultra low-dose images. The noise on the blended images was slightly higher (up to 11%) than that on the 60 keV images, for standard of care group. Noise was reduced by 18% for the blended images, as compared with 60 keV monochromatic images, in the ultra low-dose group.

Radiation dose

Respective mean $CTDI_{vol}$, size specific dose estimate, DLP and ED for standard of care and reduced dose DECT were 4.9 ± 0.9 and 1.3 ± 0.2 mGy ($p < 0.001$) (ranging from 0.65 to 1.64 mGy); 6.8 ± 0.8 and 1.8 ± 0.2 mGy ($p < 0.001$); 191 ± 39 and 51 ± 9.9 mGy.cm ($p < 0.001$); and 2.7 ± 0.5 and 0.7 ± 0.1 mSv ($p < 0.001$) (ranging from 0.39 to 0.97 mSv).

The mean ED per patient (including both standard of care and research image series) was 3.4 ± 0.7 mSv, a value lower than the average ED reported in the literature (7 mSv) for single energy chest CT scans.¹⁹

DISCUSSION

The results of our study show that a chest DECT scan can be performed at sub-mSv doses (mean ED 0.7 ± 0.1 mSv) without loss of diagnostic information in patients with BMI less than 31 kg m^{-2} . Although the ultra low dose images were noisier, no significant difference in image sharpness and lesion conspicuity

Table 4. Objective assessment of image noise, SNR and CNR on monochromatic images at 60 and 40 keV for standard of care chest DECT and reduced dose chest DECT

	Standard of care DECT		Reduced dose DECT		% difference	
	60 keV	40 keV	60 keV	40 keV	60 keV	40
Image noise						
Trachea	9.5 ± 3.2	15.1 ± 6.3	10.7 ± 4.0	19.9 ± 14.7	13%	32%
Muscle	13.4 ± 2.9	24.3 ± 6.3	23.0 ± 5.5	38.8 ± 7.0	72%	60%
Bone	27.8 ± 7.8	46.0 ± 12.0	42.4 ± 16.3	60.7 ± 12.6	52%	32%
SNR						
Trachea	112.4 ± 33.4	76.6 ± 34.8	101.0 ± 33.5	75.6 ± 46.5	-10%	-1%
Muscle	4.3 ± 1.8	2.8 ± 1.1	2.4 ± 1.1	1.6 ± 0.8	-44%	-43%
Bone	5.9 ± 2.0	5.5 ± 1.9	4.3 ± 1.6	4.5 ± 1.5	-27%	-18%
CNR						
Muscle	106.2 ± 31.9	71.6 ± 32.5	95.3 ± 30.5	69.9 ± 41.8	-10%	-2%
Bone	94.3 ± 28.9	56.6 ± 26.0	82.4 ± 25.3	51.8 ± 29.4	-13%	-8%

CNR, contrast-to-noise ratio; DECT, dual energy CT; SNR, signal-to-noise ratio.

Note: Numbers represent mean image noise (defined as the standard deviation of the voxel values), mean SNR and mean CNR and standard deviation of the mean.

was detected between the full dose and the ultra low dose protocols by four experienced readers. Since lesion conspicuity is the most important feature in lung parenchymal assessment (rather than SNR and CNR),¹⁷ the performance of the ultra low dose protocol (blended images) was deemed similar to our clinically deployed standard of care DECT protocol. To our knowledge, this is the first time that sub-mSv doses have been successfully applied to yield diagnostic image quality in a patient study using a dual source DECT scanner. Furthermore, we strongly believe that this low dose protocol can be routinely performed regardless the achievement of sub-mSv doses.

Low-dose and ultra low-dose chest CT scans have been successfully used in research studies and proven diagnostic in multiple clinical scenarios, particularly when patients need serial short-term follow-up CT scans.^{20,21} Low-dose chest CT is now mandated for lung cancer screening²² and the results of our study supports the use of DECT scanners as a screening tool for lung cancer. Moreover, the low-dose monochromatic images at 40 keV could yield a slightly superior contrast enhancement in the left pulmonary artery as compared with blended and 60 keV monochromatic standard dose images, despite the 10 s delay between the acquisitions. This indicates that DECT can enable reduction of the contrast volume in chest studies.²³ Although the generated virtual non-contrast images were not assessed in this study (given the 10 s delay between the acquisitions), there has been demonstrated that they can replace precontrast images without the radiation penalty of an extra CT acquisition in specific scenarios.²⁴ Thus, the dose reduction achieved by DECT can be even more impressive.

Our results are in accordance with recent published papers, which employed low- and ultra low-doses for *single energy* chest CT scans and reported diagnostic quality scans for both. Lee et al²⁵ showed that ultra low-dose chest CT images were diagnostic, using doses as low as 0.29 mSv in patients with BMI less than 25 kg m⁻². However, limitations regarding the detection of lesions with decreased attenuation and ground-glass nodules were found in this study. Padole et al²⁰ and Kim et al²⁶, using different iterative reconstruction techniques, reported EED doses down to 1.06 mSv (for low-dose protocols) and 0.44 mSv (for ultra low-dose protocols), respectively. Kim et al²¹ reported mean dose of 0.6 mSv for ultra low-dose chest CT scans and accuracy up to 99.5% to diagnose pulmonary infection in patients with neutropenic fever and haematological malignancy. Macri et al⁵ demonstrated that ultra low-dose chest CT scans can be performed at 0.18 mSv and still provide high-level diagnostic confidence for

the evaluation of patients with acute dyspnea. Furthermore, Rampinelli et al²⁷, in a 10-year, single centre, low-dose CT, lung cancer screening trial reported average EDs of 1.07 mSv, 1.05 mSv and 0.64 mSv for three different single energy scanners. These doses are similar to our average achieved EED (0.7 mSv), suggesting that DECT scanners can be used for lung cancer screening as well.

This study has some limitations. In order to conduct a perfectly matched standard dose and sub-mSv dose CT study, the research component of this examination was performed at the end of the patient's clinical CT examination, delivering a clinically unnecessary additional radiation dose. This extra acquisition limited our sample size. Therefore, our findings reflect just a preliminary experience from a small cohort. Nevertheless, our sample size is similar to previously published CT radiation dose reduction studies in chest and abdomen.^{28,29} Moreover, only patients with BMI less than 31 kg m⁻² (ranging from 19.8 to 30.5 kg m⁻²) were included in this study. It is uncertain how SAFIRE will perform or achieve sub-mSv doses in patients with BMI greater than 31 kg m⁻². Although we used a single setting of iterative reconstruction (SAFIRE S3) in our study, this setting sufficed for all patients and is clinically used in our current institutional standard of care protocols. A slight difference in the enhancement of vascular structures was observed between the standard and ultra low dose blended images due to the 10 s delay. Although this difference was not taken into account in the overall image quality assessment, it may represent another potential limitation of the study. Last, further studies are necessary to assess how the quantitative measurements of iodine will perform when low radiation doses are applied for chest DECT scans.

In summary, diagnostic contrast-enhanced DECT of the chest can be performed at sub-mSv doses, down to mean CTDI_{vol} 1.3 mGy and DLP 51 mGy.cm in patients with BMI <31 kg m⁻². The ultra low dose DECT images were deemed adequate for lesion detection and visualization of subtle anatomic structures.

CONSENT

This study was approved by Institutional Review Board with written informed consent from each participating subject. It was conducted in accordance with the Health Insurance Portability and Accountability Act.

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