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ORIGINAL ARTICLE / *Abdominal imaging*

Virtual unenhanced phase with spectral dual-energy CT: Is it an alternative to conventional true unenhanced phase for abdominal tissues?

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Projection/methods;
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Abstract

Purpose: To compare attenuation measurements and image quality of virtual unenhanced phase (VUP) images with those of conventional true unenhanced phase (TUP) images on spectral dual energy computed tomography (DECT) with dual layer detector on abdominal tissues and to assess potential reduction in radiation dose.

Material and method: A total of 295 patients (185 men, 110 women; mean age 61 ± 17.6 [SD] years [range: 17—95 years]) who had undergone abdominal or thoraco-abdominal CT with pre- and post-contrast imaging (portal phase) with spectral DECT with dual layer detector were retrospectively analyzed. VUP images based on portal-venous phase DECT acquisition were generated. Regions of interest were defined in abdominal tissues (liver, spleen, kidney, muscle and fat) by two independent readers. Inter-technique agreement (VUP images vs. TUP images) on attenuation measurements was assessed. Signal-to noise ratio (SNR) and image quality of TUP and VUP images were compared. The radiation dose delivered to patients was compared with the radiation dose of protocols without TUP images.

Results: A total of 9880 ROIs were drawn in the abdominal tissues. The difference in mean attenuation values between TUP and VUP images was less than 15 HU in 98.3% and less than 10 HU in 92.3% of all measurements. VUP images overestimated attenuation in fat comparatively to TUP images. Image quality was evaluated as good or excellent in 77% (37/48) of TUP images and 54% (26/48) of VUP images. Using VUP images instead of TUP images could decrease the radiation dose by 32%.

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Conclusion: VUP images demonstrate good agreement with TUP images in different abdominals tissues and can be obtained with similar image quality as TUP. VUP images appear as an alternative to TUP images, resulting in reduction of radiation dose delivered to the patient.

Abbreviations

BMI	Body mass index
CT	Computed tomography
DLP	Dose length product
HU	Hounsfield unit
kVp	Kilovolt peak
ROI	Region of interest
SBI	Spectral database image
SNR	Signal-to-noise ratio
TUP	True unenhanced phase
VUP	Virtual unenhanced phase

Introduction

The use of true non-contrast (TUP) images derived from computed tomography (CT) acquisition is often needed before intravenous administration of iodinated contrast material in many indications [1,2]. TUP images allow detecting hematoma or calcification, assessing metabolic and morphological change in liver parenchyma as well as measuring pre-contrast absolute attenuation values. Dual-energy CT (DE-CT) is characterized by an acquisition using different energy levels (low and high) and enables material decomposition allowing to generate an ''iodine map'' [3]. It provides, with the help of specific algorithms, virtual unenhanced phase (VUP) images, in which the attenuation due to the iodine content is subtracted from contrast-enhanced images. DECT can be performed using different technologies including dual-source CT, dual layer detector and rapid switching of X-ray tube potential. They all generate two datasets at different energies in a single acquisition. The most recent DECT technology consists of a system composed with dual layer detectors (''sandwich'' mode) [4]. Dual layer detector CT scanner is composed of an X-ray tube that emits a polychromatic beam that is used to expose a detector consisting of two layers of scintillators. The two layers of scintillators are directly on top of one another. The upper layer is made of low-density scintillator (Yttrium-based), sensitive to low energies; and the lower layer is made of high-density gadolinium oxysulfide (GOS) scintillator, sensitive to high energies [4,5]. In addition, true routine diagnostic CT images are directly obtained from the scanner by combined data from the top and bottom layers. This is different from the other currently available technologies, where low- and high- energy images are obtained and mixed at different ratios to obtain a surrogate ''conventional/combined/blended'' image set [6].

Our hypothesis in this study was that VUP DECT images might replace TUP DECT images. If validated, the technique might retrospectively help characterize incidentaloma detected on enhanced phase images and also reduce the cost and the time of CT examination as well as radiation dose delivered to the patient. The latter is important because it reduces the risk to develop malignant tumor due radiation from medical imaging [7]. To our knowledge, only two studies have compared TUP images to VUP images on spectral DECT with dual layer detectors [8,9].

The aim of this study was to compare attenuation measurements and image quality of VUP DECT images derived from portal phase with TUP DECT images on spectral DECT with dual layer detectors.

Materials and methods

Study population

This retrospective study was approved by the local institutional review and informed consent was waived. A total of 3020 patients who had abdominal or thoraco-abdominal CT with pre- and post-contrast CT imaging (portal phase) between May and October 2016 were initially retrieved. Exclusion criteria were:

- absence of TUP images or absence of portal phase or presence of a single arterial phase;
- presence of abnormal findings on CT images.

A total of 2725 patients were thus excluded. Fig. 1 shows patient inclusion into the study.

The study population included 295 patients with a mean age of 61 ± 17.6 (SD) years (range: 17—95 years). There were 185 men (mean age, 62 ± 17.3 [SD] years; range: 17—95years) and 110 women (mean age, 57 ± 18.3 [SD] years; range: 18—92 years).

CT acquisition and reconstruction

All examinations were performed on an IQon® spectral CT scanner (Philips Healthcare) with the patient in prone position. First, TUP images of the abdomen were obtained from the diaphragm to the symphysis pubis, with a collimation of 64×0.625 mm, a pitch of 1.079 and with a 120 kVp voltage. The mAs were automatically adapted with the dose modulation. The rotation time of the gantry was 0.4 s. Then portal

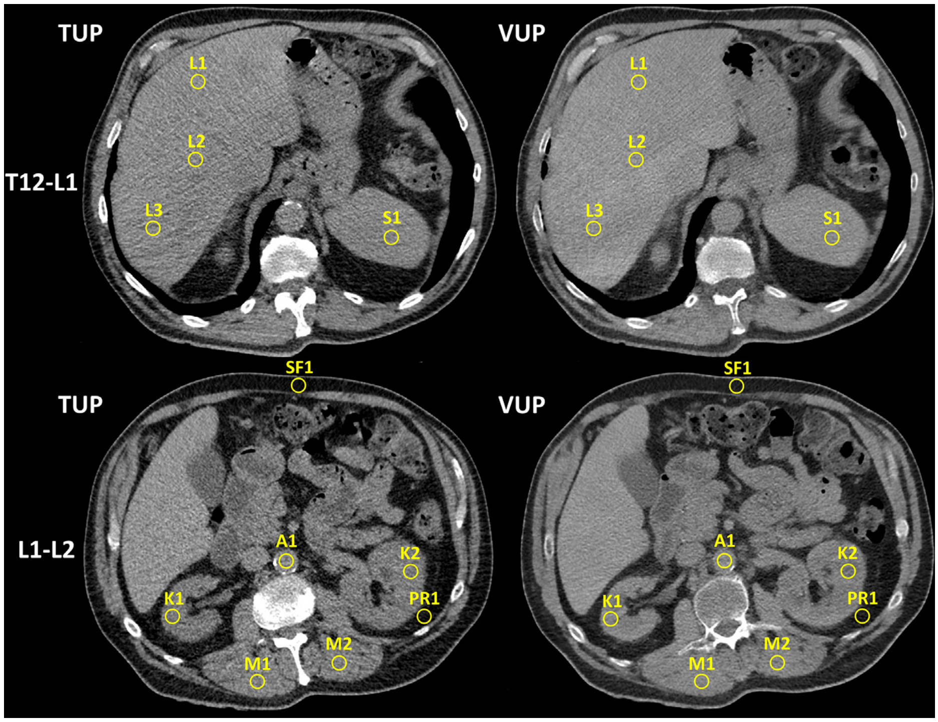

Figure 1. Flowchart of patient inclusion. DECT indicates spectral dual energy computed tomography.

phase images were obtained with the same parameters 70—80 s after the initiation of intravenous administration of 80 to 120 mL of iodinated material contrast (iobitridol, Xenetix 350®, 350 mg of iodine/mL, Guerbet) at a flow rate of 2 to 3.5 mL/sec followed by 30 mL of saline. TUP and VUP images were reconstructed at 3-mm slice thickness with a hybrid iterative reconstruction algorithm (iDose® level 4, Philips Healthcare) [10].

Image analysis

The spectral DECT generated conventional images obtained by the combination of the low and high energy absorption data and spectrally decomposed images. These datasets were stored as spectral base images dicom files, from which VUP could be derived. Spectral database images (SBI) were transferred to a workstation (IntelliSpace® Portal Workstation, Philips Healthcare) where VUP reconstructions were rebuilt to 3 mm slice thickness from the portal phase and analyzed on the picture archiving and communication system (PACS) viewing station. VUP was available about 2—5 minutes at the end of the acquisition for an abdominal CT, with the exact timing depending on the number of reconstructed slices.

Quantitative analysis

TUP and VUP images were reconstructed using a dedicated software (4.7.0. Philips Healthcare) used for the spectral reconstructions at ISP workstation, then send on the PACS viewing station. Several regions of interest (ROI) were drawn by two readers (S.J. and C.D.) with 5- and 20-years of experience in radiology on TUP and VUP images on the PACS viewing station. Circular ROIs were delineated on 5 different tissue types including liver, spleen, kidney, muscle and fat. On the section at the level of the 12th thoracic vertebra (T) and the 1st lumbar vertebra (L1), 3 ROIs were randomly drawn on the hepatic parenchyma, avoiding vessels, and 1 ROI on the spleen. On the section on L1-L2 level, one ROI on interpolar region of kidney and paraspinal muscle bilaterally, one ROI on perirenal and subcutaneous fat were drawn (Fig. 2). Each ROI had an area of at least 100 mm^2. The attenuation values (in HU) were measured on the ROIs on both TUP and VUP images and further compared. Retrospective analysis of the images was performed to elucidate the causes of marginal differences in the liver (12 patients).

Image data from the 247 selected patients for the quantitative analysis were read in consensus by the same two readers. A total of 9880 ROIs were analyzed (2964 in the liver, 988 in the spleen, 1976 in the kidneys , 1976 in the muscles, 988 in the subcutaneous fat and 988 in perirenal fat).

Qualitative analysis

Qualitative analysis was performed in consensus by the two readers on 48 patients. This subjective analysis was based on a visual assessment of image quality taking into account:

- the suppression of the contrast in the vessels (portal trunk, hepatic and renal vessels);
- the appearance of the hepatic parenchyma;
- the cortico-medullary differentiation of the kidneys.

TUP and VUP image quality was rated using a 4 point Likert scale, from 1 to 4 as follows: 4 = excellent, no significant artifacts; 3 = good, minor artifacts, 2 = fair, some artifacts but most regions readable, 1 = poor, severe artifacts, many regions unreadable. The proportion of each rating of image quality for TUP and VUP was assessed. Then the proportion

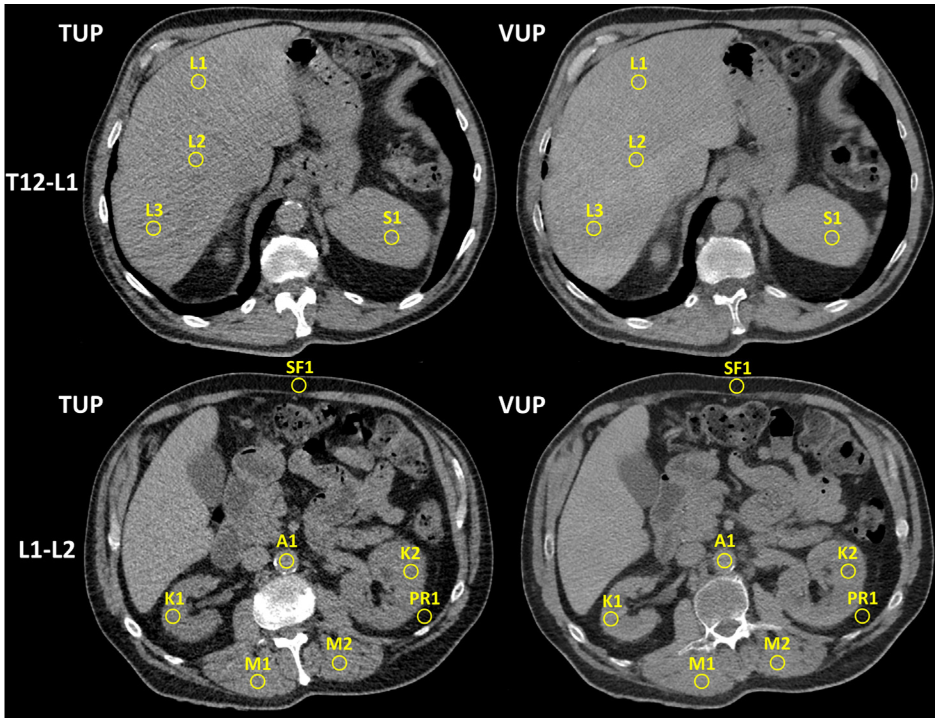

Figure 2. Figures shows regions of interest (ROI) placement for measurements. A and C correspond to true unenhanced phase (TUP) images in the axial plane of the abdomen. B and D correspond to virtual unenhanced phase (VUP) images in the axial plane generated from the spectral DECT with dual layer detector obtained during the portal phase. At the level of T12-L1 (A, B), ROIs were drawn in the liver (L1, L2, L3) and spleen (S1). At level of L1-L2 (C, D), ROIs were drawn in the kidney (K1, K2), subcutaneous and perirenal fat (SF1, PR1) and paraspinal muscle (M1, M2). Aorta (A1) data was not analyzed. ROIs were first drawn on TUP images, then, copied/pasted on the VUP images, and manually repositioned when the anatomical matching between imaging slices was not enough accurate).

of low quality TUP images (scored 1 or 2) was assessed only when low quality VUP images (scored 1 or 2) were present. Signal-to-noise ratio (SNR) of TUP and VUP images were compared. Standard deviation of the noise was assessed in the surrounding air. Finally, for 100 patients randomly selected from our cohort, the total dose delivered to the patient (DLP) during the different phases were collected.

Statistical analysis

Attenuation measurements of TUP and those of VUP images were compared using the Wilcoxon's signed rank test because the data were not normally distributed using the D'Agostino-Pearson test. Then, inter-technique agreement (TUP vs. VUP images) on attenuation measurements was evaluated using the Bland-Altman diagram. From each diagram, the mean bias (indicating a potential under- or overestimation of one technique compared to another), the regression line of differences (indicating differences proportional with the magnitude of the measurements) and the limits of agreement (indicating the range within which we expect 95% of future differences in measurements between techniques to lie; the narrower this interval, the better the agreement is) were assessed. The percentage of differences measurements lying within the tolerance intervals proposed by Ananthakrishnan et al. was also reported [8]. Distribution of image quality ratings was studied using column bars. Differences in image quality ratings between TUP and VUP images were assessed using the Wilcoxon's signed rank test. Comparison between SNR_{TUP} and SNR_{VUP} were performed using paired Student *t* test. The radiation dose in biphasic and triphasic protocols with TUP images was compared to the dose of the same protocols without TUP images. The difference in radiation dose between them was assessed using Wilcoxon's signed rank test.

A *P* value < 0.05 was regarded as statistically significant for all tests cited above. All analyses were performed under Statsdirect Statistical Software version 3.1.14 (http://www.statsdirect.com/).

Results

Attenuation value measurements

The results of attenuation value measurements are reported in Table 1. TUP and VUP images demonstrated statistically significant differences in attenuation in the spleen ($P < 0.001$) and muscle ($P < 0.0001$) (small differences ranging from +1.1HU to −0.6HU) as well as in the kidney ($P < 0.0001$), perirenal fat and subcutaneous fat ($P < 0.0001$) (larger differences ranging from +7.2HU to −14.4HU). Attenuation value measurements in absolute value were higher in TUP images except in the muscle (Table 1).

Inter-technique agreement

Bland-Altman diagrams for each tissue are reported in Fig. 3. The width of agreement intervals had the same order of magnitude whatever the tissue studied (when recentered

Table 1 Median attenuation values (in HU) and mean signal-to-noise ratios (unitless) of abdominal organs with virtual unenhanced phase (VUP) and true unenhanced phase (TUP) images.

	HU^{TUP}	HU^{VUP}	*P* value	SNR^{TUP}	SNR^{VUP}	*P* value	Mean difference
Liver	55 (55; 56)	55 (55; 56)	0.1006	4.6 (4.3; 4.9)	5.0 (4.7; 5.3)	0.0087	−0.4 (−0.7; −0.1)
Spleen	48 (48; 48)	47 (46; 47)	< 0.0001	4.0 (3.7; 4.2)	4.2 (3.9; 4.4)	0.2187	−0.2 (−0.4; +0.1)
Kidney	33 (32; 33)	29 (28; 29)	< 0.0001	2.7 (2.6; 2.9)	2.5 (2.3; 2.7)	0.0374	+0.2 (+0.0; +0.5)
Muscle	46 (45; 47)	47 (46; 47)	< 0.0001	3.5 (3.2; 3.8)	4.0 (3.7; 4.3)	0.0005	−0.5 (−0.7; −0.2)
Subcutaneous fat	−110 (−111; −109)	−96 (−96; −95)	< 0.0001	8.8 (8.1; 9.4)	8.3 (7.7; 8.9)	0.1175	+0.4 (−0.1; +1.0)
Perirenal fat	−104 (−105; −103)	−91 (−92; −90)	< 0.0001	8.4 (7.7; 9.0)	8.0 (7.4; 8.6)	0.1712	+0.4 (−0.2; +1.0)

Results are expressed as median. Numbers in parentheses are first (Q_1) and third (Q_3) quartile. VUP indicates virtual unenhanced phase images. TUP indicates true unenhanced phase.

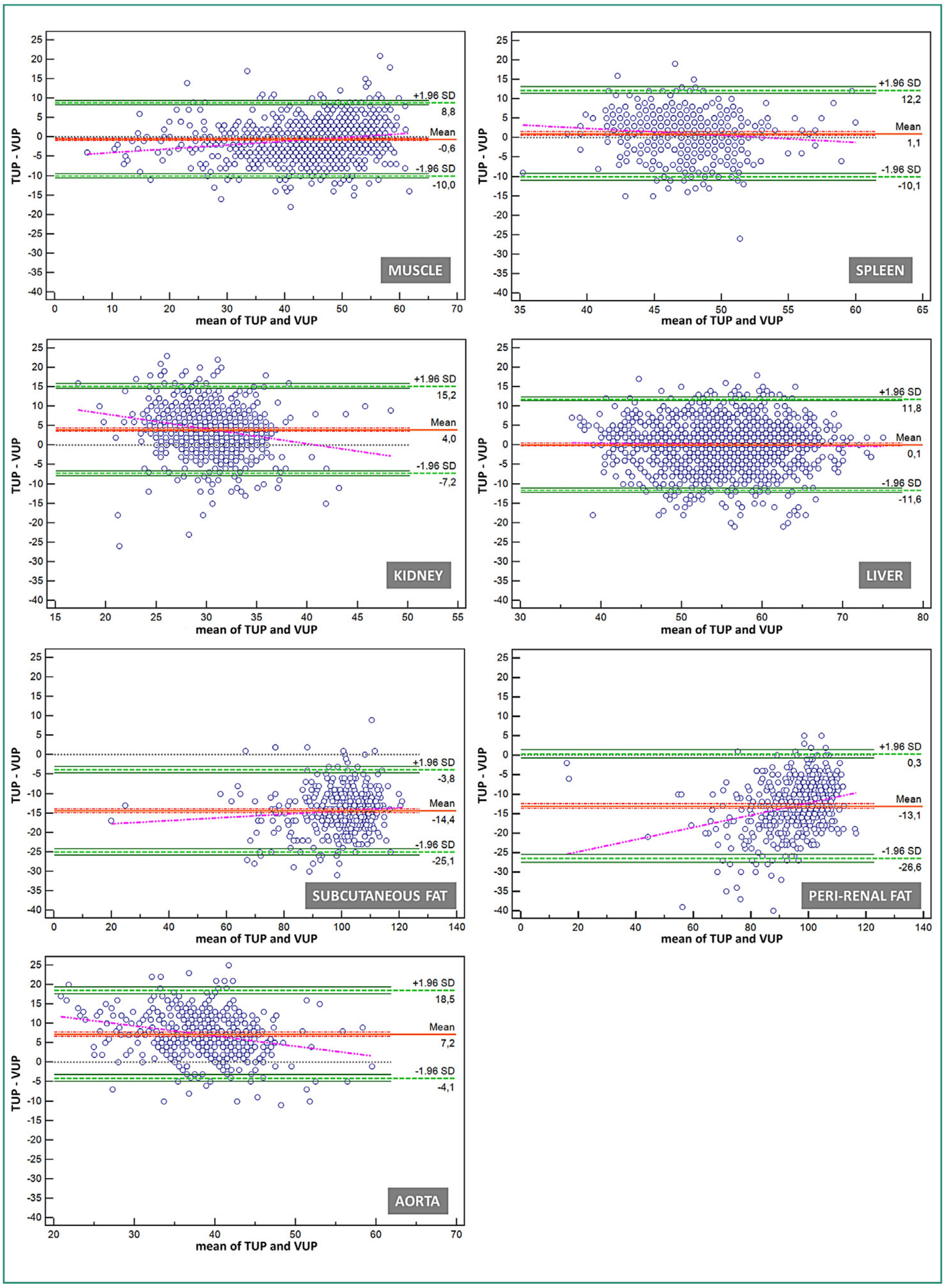

Figure 3. Bland-Altman diagrams show agreement for attenuation measurements between true unenhanced phase (TUP) and virtual unenhanced phase (VUP) images in various organs and areas. The mean bias and agreement interval (and their 95% confidence intervals) as well as the regression line of differences (helping to detect a proportional difference over the range of observed HU values) are given. TNC indicates true unenhanced phase (TUP). VNC indicates virtual unenhanced phase (VUP).

around the mean bias: TUP-VUP $_{muscle}$ ranged between −9.4HU and +9.4HU], TUP-VUP $_{spleen}$ ranged between −11.2HU and +11.2HU, TUP-VUP $_{kidney}$ ranged between −11.2HU and +11.2HU, TUP-VUP $_{liver}$ ranged between −11.7HU and +11.7HU, TUP-VUP $_{perirenal\ fat}$ ranged between −13.5HUand +13.5HU, TUP-VUP $_{subcutaneous\ fat}$ ranged between [−14.5HU; +14.5HU. The slope of the regression line was different from zero in each tissue except for the subcutaneous fat (slope $_{muscle}$ = 0.355, $P < 0.0001$; slope $_{spleen}$ = −0.057, $P = 0.035$; slope $_{kidney}$ = −0.120, $P < 0.0001$; slope $_{liver}$ = −0.064, $P = 0.025$; slope $_{subcutaneous\ fat}$, $P = 0.053$; slope $_{perirenal\ fat}$ = 0.487, $P < 0.0001$) indicating that, in these tissues, the bias varied with the magnitude of attenuation measurements. However, the slopes values of the regression were < 1.0, showing that these proportional differences were small (Fig. 3).

The percentage of difference measurements for each tissue lying within the predefined tolerance intervals are reported in Table 2. A tolerance of ± 15 HU showed that TUP images and VUP images were interchangeable techniques (as soon as the bias has been taken into account), while a more restrictive tolerance of ± 10 HU limits this

Table 2 Percentage of differences in measurements (in Hounsfield units [HU]) between virtual unenhanced phase (VUP) and true unenhanced phase (TUP) images.

	[−15 HU; +15 HU]	[−10 HU; +10 HU]
Liver	97.6%	90.4%
Spleen	99.0%	91.2%
Kidney	98.3%	93.3%
Muscle	99.4%	95.1%
Perirenal fat	96.5%	88.2%
Subcutaneous fat	98.2%	92.4%

Each tolerance interval is recentered around the mean bias estimated from the Bland-Altman diagram before calculating the percentage.

interchangeability to the analysis of the muscle (if a maximal threshold of 5% of marginal differences is set). More marginal differences (beyond the tolerance intervals) were observed in the perirenal fat and liver.

Image quality

Analysis of image quality is reported in Fig. 4. TUP images demonstrated higher quality ratings compared to VUP images ($P = 0.0082$), though VUP images had either an excellent or good quality in 54% (26/48) of patients. When TUP image quality was rated excellent, VUP quality was excellent in 41% (7/17), good in 35% (6/17) and fair in 24% (4/17) of examinations.

When VUP image quality was low, TUP image quality was low in 41% (9/22) of examinations. A total of 6/48 (13%) examinations were non-interpretable with VUP (while being interpretable with TUP) and 1/48 (2%) examination was non-interpretable with TUP (while being interpretable with VUP). However, the differences between TUP and VUP on the number of non-interpretable examination were not significant ($P = 0.125$).

SNR

Mean SNR values are reported in Table 1. TUP and VUP images demonstrated statistically significant differences in SNR in the liver, kidney and muscle. SNR of TUP images were higher in the kidney than in other abdominal tissues, while SNR of VUP images was higher in the liver and muscle than in the other abdominal tissues.

Radiation dose

Analysis of doses is reported in Table 3. When TUP images were not performed, a significant reduction in dose was observed in both biphasic and triphasic protocols, with a reduction in dose of 48.5% for biphasic ($P < 0.0001$) and 31.2% for triphasic protocols ($P < 0.0001$) compared to protocols including TUP images.

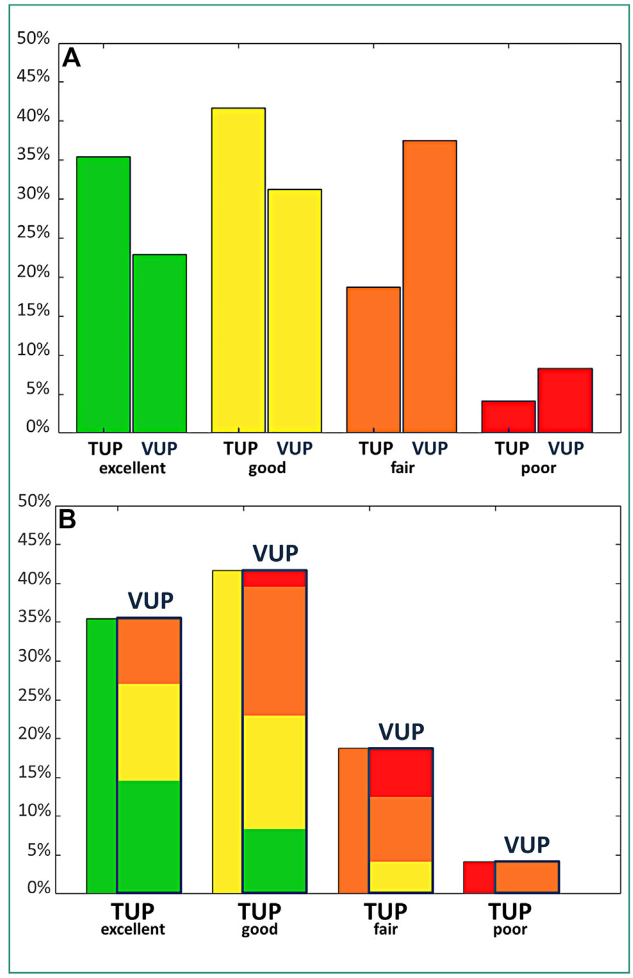

Figure 4. Column bars shows results of image quality analysis. A) Distribution of ratings. True unenhanced phase (TUP) images demonstrate significantly higher ratings compared to virtual unenhanced phase (VUP) images ($P = 0.0082$), though VUP images had either an excellent or good quality in 54% patients. B) Distribution of VUP ratings within each TUP rating. When TUP image quality was rated excellent, VUP quality ranged from excellent (41%), good (35%) to fair (24%). When TUP image quality was poor, VUP quality was fair. TNC indicates true unenhanced phase (TUP). VNC indicates virtual unenhanced phase (VUP).

Discussion

In this study we performed a quantitative and qualitative comparison of TUP and VUP abdominal images obtained with a spectral DECT with dual layer detector. A high accuracy of mean attenuation values of VUP images compared to TUP images was observed for all tissues. TUP and VUP images were similar in 98.3% with a tolerance interval [−15HU; + 15HU] and in 92.3% with a tolerance interval [−10HU; + 10HU] of all measurements. Results on the inter-technique agreement are consistent with those of prior studies [8,9]. Ananthakrishnan et al. showed that VUP and TUP images are equivalent in 92.6% of patients in all organs of the abdomen with a tolerance interval [−15HU; + 15HU] and in 75.2% of patients in all organs studied with a tolerance range of [−10 HU; +10 HU] [8]. Sauter et al. showed that difference between TUP and VUP images was 10HU or

Table 3 Median values of radiation dose as expressed as dose length product (DLP) and percentage of dose reduction.

	DLP (mGy*cm)	DLP-TUP	Median difference	Dose reduction (%)
Biphasic protocol	505 (414; 672)	280(222; 352)	+245 (+214; +292)	48.51(42.37, 57.82)
Triphasic protocol	632 (508; 845)	452(366; 584)	+197 (+176; +223)	31.17(27.84, 35.28)

Data are expressed as median. Numbers in parentheses are first (Q_1) and third (Q_3) quartile. DLP indicates dose length product. TUP indicates true unenhanced phase images. A significant dose reduction is observed for both protocols when TUP is not performed ($P < 0.0001$).

less in over 80% and 15HU or less in 92% of all measurements [9]. The differences in our results may be due to the difference in size of the cohort studied; 247 for our study against 46 patients for Ananthakrishnan et al. [8] and 62 patients for Sauter et al. [9].

We found that VUP images demonstrated a significant mean bias compared to TUP images in attenuation measurements. However, this mean bias is large in fatty tissues only. We also found that the agreement intervals on attenuation measurements have similar width whatever the studied tissue (meaning that differences in measurements between techniques were similar regardless the organ) and were included within a tolerance interval of [−15HU; +15HU] (indicating that measurements from both techniques are equivalent to ±15HU). However, a stricter tolerance of [−10HU; +10HU] between both techniques, with at best 5% of marginal differences, may not allow concluding that VUP images can replace TUP images.

The observation of overestimation (a mean positive bias) demonstrated by VUP images in fat has been reported by Ananthakrishnan et al. [8]. Sauter et al. found a difference of more than 15 UH in 12% of all measurement for fat [9]. This bias may be explained mainly by the fact that fat is not part of the material decomposition algorithm including the iodine and water pair used in the VUP reconstruction. Although the spectral technologies differ, our results are similar to some studies that have shown a good agreement between TUP and VUP images [11—14] and a good image quality on VUP images [8,12,15,16]. Of note, Durieux et al. also observed an overestimation in attenuation in VUP images on retroperitoneal fat [14]. However, this experimentation was performed with another dual energy CT technique.

In this study, when TUP image quality was rated excellent, VUP image quality was rated excellent or good (76%), which is lower than the 85% reported by Ananthakrishnan et al. [8]. This difference in rating may result from the experience and familiarity of the reader with one or the other type of reconstruction, the difference in scale of the qualitative analysis in both studies (4 vs. 5 points), as well as the subjective nature of qualitative scoring. Though there was no significant difference between TUP and VUP images on the proportion of examinations that remain non interpretable, this result should be interpreted with caution because it was obtained from a small study sample.

We observed that the lower quality of VUP reconstruction was due to the incomplete subtraction of iodine in some patients, mainly in the hepatic veins and in the renal cortical area. Previous studies have shown an inhomogeneous subtraction of iodine on VUP images [15], especially in the portal trunk, hepatic veins or inferior vena cava, which are areas of high iodine concentration [17]. Some factors may influence iodine subtraction including patient size, beam hardening artifacts, high iodine concentrations [11,15], and post-processing parameters of the software used to create the VUP images [16]. Final VUP image depends on quality and dose parameters of the initial CT acquisition but does not take into account the cardiac rhythm nor the weight of the patient. Quantification inaccuracies of VUP images tend to be worst at large patient size and low radiation dose on TUP [18].

In our study, we found a SNR in VUP images greater than that in TUP images in the liver and muscle. This is in agreement with prior studies [11,12,15,19,20]. This higher SNR may be due to the noise filter added in the post-processing of the spectral images which is responsible for a smoother aspect of the images [11]. Our study also shows that VUP images have a lower SNR in the kidneys. This could be related to an incomplete subtraction of iodine, cortical medullary differentiation visualized on the portal phase may persist in a number of cases in VUP images affecting the attenuation values.

VUP has a potential advantage in reduction of radiation dose delivered to the patient. In our study, the radiation dose reduction due to TUP images is 48.5% (42.4—57.8%) in biphasic examinations and 31.17% (27.84%—35.28%) in triphasic examinations. Previous studies using other spectral technologies have also reported dose reduction due to TUP images suppression in triphasic examinations of 35% [11,16], 34% [12], 30% [15,21] and 25% [13].

Our study has several limitations. First, some parameters were not analyzed, in particular, the body mass index and cardiac function of the patients, the amount of intravenous contrast material and the specific acquisition protocols. It may be assumed that these parameters may influence the degree of enhancement in structure/tissues. Second, VUP reconstructions were only obtained from portal venous phase data.

In conclusion, we found a good agreement on attenuation measurements between VUP and TUP images on patients who had abdominal or thoraco-abdominal DECT with unenhanced portal phase images, in most abdominal tissues with overestimation in fatty tissues. Although VUP image quality was lower than that of TUP images, VUP images showed excellent or good quality in 54% of patients. VUP images may be an alternative to TUP images with a decrease in radiation dose. However, further studies are needed assess the potential of VUP images in the detection of pathological lesions.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s).

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CRediT authorship contribution statement

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

All authors certify that they have participated sufficiently in the work including participation in the concept, design, analysis, writing, or revision of the manuscript.

Sanaa Jamali and Cristina Anca Dragean were involved in planning this study, performed the analysis and writing. Sanaa Jamali was the main writer. Nicolas Michoux worked on the statistical analysis and generation of data graphs. Emmanuel Coche and Cristina Anca Dragean provided guidance and advices. All authors discussed the results and contributed to the final manuscript.

Disclosure of interest

The authors declare that they have no competing interest.

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