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Reduction of contrast medium volume in abdominal aorta CTA: Multiphasic injection technique versus a test bolus volume

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ABSTRACT

Objective: The purpose of this study is to reduce the administered contrast medium volume in abdominal CTA by using a test bolus injection, with the preservation of adequate quantitative and qualitative vessel enhancement.
Study design: For this technical efficacy study 30 patients, who were referred for a CTA examination of the abdominal aorta, were included. Randomly 15 patients were assigned to undergo a multiphasic injection protocol and received 89 mL of contrast medium (Optiray 350) (protocol I). Fifteen patients were assigned to the test bolus injection protocol (protocol II), which implies injection of a 10 mL test bolus of Optiray 350 prior to performing CTA with a 40 mL of contrast medium. Quantitative assessment of vascular enhancement was performed by measuring the amount of Hounsfield Units in the aorta at 30 positions from the celiac trunk to the iliac arteries in both groups. Qualitative assessment was performed by three radiologists who scored the images at a 5-point scale.
Results: Quantitative assessment showed that there was no significant difference in vascular enhancement for patients between the two protocols, with mean attenuation values of 280.9 ± 50.84 HU and 258.60 ± 39.28 HU, respectively. The image quality of protocol I was rated 4.31 (range: 3.67/5.00) and of protocol II 4.11 (range: 2.67/5.00). These differences were not statistically significant.
Conclusion: This study showed that by using a test bolus injection and the administration of 50 mL of contrast medium overall, CTA of the abdominal aorta can reliably be performed, with regard to quantitative and qualitative adequate vessel enhancement.

1. Introduction

With the advent of multi-slice CT (MDCT) scanner and the sophisticated CT reconstruction algorithm, CT is increasingly used to evaluate patients with vascular diseases. It has many advantages over the conventional catheter angiograms: non-invasiveness, short acquisition time, multiple viewing methods and directions, low costs and dose reduction [1].

Nowadays 64 or 256 MDCT allows to obtain an entire scan of the abdominal aorta in about 5 s. As a result, scan timing becomes far more critical and challenging than with older and slower CT scanners [2]. The other consideration with this challenge is that the short scanning time of MDCT may prove the opportunity to a more efficient contrast use, and improvement of contrast enhancement. With MDCT, the amount of contrast medium injected during some clinical applications may be reduced without decreasing contrast enhancement [3].

Contrast-induced nephropathy (CIN) is a well-recognized complication of radiographic contrast administration and is the third leading cause of hospital-acquired renal insufficiency [4]. It is most commonly defined as acute renal failure occurring within 48 h of exposure to intravascular radiographic contrast material that is not attributable to other causes [5]. CIN leads to prolonged hospitalization, dialysis and increased mortality [6]. The incidence of CIN is <5% in patients without risk factors, however is increased among patients with chronic kidney disease, particularly those who have

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Table 1
In- and exclusion criteria.

Inclusion criteria	Exclusion criteria
Referred for CTA of the abdominal aorta	Allergy contrast medium
Mentally competent	Mentally incompetent
Written informed consent	Known arrhythmias or other heart disorders
≥18 years	<18 years
Kidney function ≥ 60 GFR	Kidney function < 60 GFR
	Pregnancy or lactation

diabetes mellitus [6–8]. The incidence may be as high as 50% in patients with multiple risk factors as, advanced age, congestive heart failure, nephrotoxic drug use, hypovolemia and excessive contrast medium use [9].

Results of a recent study involving the use of an exponentially decelerating (multiphasic) injection protocol demonstrated that enhancement patterns of a standard uniphasic injection protocol and a multiphasic injection protocol were quantitatively as well as qualitatively comparable. By using a multiphasic injection technique with CTA of the abdominal aorta a reduction of 11 percent of contrast medium can be realized [10]. The purpose of this study is to further decrease the injected contrast medium volume in CTA by using a test bolus prior to injection of the total amount of contrast medium.

2. Materials and methods

2.1. Study design

A randomized, double blind technical efficacy study in patients referred for CTA of the abdominal aorta was performed. The study protocol was approved by the institutional ethical review board. Indications for referral were preoperative work-up in abdominal aortic aneurysm (AAA), postoperative AAA control, and imaging of the renal and gastrointestinal arteries. Therefore, patients with stents, calcifications and aneurysmal dilatation were all included. In total, 30 patients who met the inclusion and exclusion criteria (Table 1) were included. Of all patients participating in this study, weight and height were noted and there body mass index (BMI) was determined. After providing written informed consent, patients were randomized into two different injection protocol groups. Prior to each scan a blinded envelop was taken, containing a note with protocol I or protocol II. Fifteen patients were scanned according to the multiphasic injection protocol (protocol I) and received 89 mL of Ioversol (i.e., Optiray 350 (350 mg of iodine per mL), Mallinckrodt Medical B.V., Petten, The Netherlands) [10]. Fifteen patients were assigned to the test bolus injection protocol (protocol II), resulting in the administration of 50 mL Optiray 350. In both groups the contrast medium was injected via an 18-gauge intravenous catheter in the medial cubital vein at the elbow, using a dual head contrast delivery injector (OptiVantage™ Injection System, Tyco Healthcare Mallinckrodt, St Louis, United States).

2.2. Protocol I

Patients in the protocol I group were injected using an exponentially decelerating (multiphasic) rate. 89 mL Optiray 350 was injected for 25 s, starting at 4.0 mL/s and decreasing exponentially to 3.1 mL/s by the end of the injection [10]. The injection of the contrast medium was immediately followed by a bolus of 20 mL saline. The decelerating injection was performed by the dual head injector of Tyco Healthcare Mallinckrodt, using the Timing Bolus™ Feature software.

With the use of bolus tracking the CT scanner started scanning 5 s after reaching the threshold of 120 Hounsfield Units (HU). The region of interest (ROI) during the bolus tracking scan was placed in the descending aorta at the level of the renal arteries.

2.3. Protocol II

Patients in this group were injected at a constant rate of 4 mL/s and with the use of a test bolus injection protocol. As described in literature [11], the test bolus method is based on injecting a small amount of contrast medium (10 mL Optiray 350), followed by injection of a saline bolus of 10 mL, prior to performing diagnostic CT with a full bolus of 40 mL Optiray 350. The full bolus injection was immediately followed by a bolus of 20 mL saline with the same injection rate. Immediately following the test bolus injection, several low-radiation-dose scans are taken at a ROI placed over the descending aorta at the level of the renal artery. A time-enhancement curve is obtained by measuring the enhancement within the ROI. The contrast material arrival time was determined from the time to peak enhancement and was used to estimate scan delays for full-bolus diagnostic CT. Time to peak enhancement of the test bolus helps adjust for individual variations in acquisition timing.

2.4. CT image acquisition

The patients were scanned using a multidetector CT (MDCT) scanner (SOMATOM Definition Flash, Siemens AG, Erlangen, Germany, 256 slice). CT scan parameters were: rotation time, 0.33 s; beam collimation, 256 mm × 0.6 mm (128 mm × 0.6 mm, *z*-flying focal spot technology); reconstruction section thickness, 3 mm; tube voltage, 120 kV; helical pitch, 1.2; table speed, 6 cm/s; mean total DLP, 482 mGy cm; mean effective dose, 7.2 mSv; ref output, 148 mA s; acquisition time, range 5–8 s. Both protocol groups were scanned with the same CT parameters.

2.5. Assessment of vascular enhancement

2.5.1. Quantitative assessment

Parameters obtained from the CTA scans were used to compare the quality of the images. The mean attenuation value in HU of a single circular ROI was measured at 30 positions in the abdominal aorta and iliac arteries, starting from the celiac trunk with a distance of about 7.5 mm between each ROI. Attenuation values in the left and right external iliac arteries were averaged. Additional analysis of the main abdominal arteries arising from the aorta was performed. The mean attenuation value in HU of a single ROI was measured 3 times at 5 different positions: in the celiac trunk, renal arteries, and superior and inferior mesenteric arteries.

The ROIs were selected in such a way that it is not too small to be affected by pixel variability and not too large so as to approach the vessel wall. Calcifications of the aortic wall and soft plaques were carefully avoided. With the software used (SyngoVia, Siemens AG, Munich, Germany), it was always possible to position the ROI perpendicular to the long axis of the blood vessel, resulting in a ROI with a maximum diameter. For each patient the mean attenuation value was calculated.

Difference in intravascular enhancement in patients with abdominal aortic aneurysm was compared with the others in each group.

2.5.2. Qualitative assessment

Qualitative assessment of the vascular enhancement was performed by three experienced radiologists, with an average working experience of 24 ± 5.29 years between them, who were unaware of each other's findings. They scored the images visually with respect to diagnostic usefulness and interpretability with the use

Table 2
Demographic data of the study population.

	Protocol I ($n=15$)		Protocol II ($n=15$)		All ($n=30$)	
Gender						
Male	10	(66.66%)	9	(60.00%)	19	(63.33%)
Female	5	(33.33%)	6	(40.00%)	11	(36.66%)
Age (*years*)						
Mean (SD)	68.60	(9.05)	69.47	(10.96)	69.03	(9.89)
Median	68.00		70.00		70.00	
Min/max	47.00	83.00	39.00	85.00	39.00	85.00
Height (m)						
Mean (SD)	1.71	(0.07)	1.69	(0.07)	1.70	(0.07)
Median	1.70		1.69		1.70	
Min/max	1.50	1.84	1.60	1.86	1.50	1.86
Weight (kg)						
Mean (SD)	83.33	(21.41)	71.47	(13.36)	77.40	(18.54)
Median	74.00		65.00		74.00	
Min/max	55.00	140.00	54.00	96.00	54.00	140.00
Body mass index (kg/m^2)						
Mean (SD)	28.24	(5.85)	24.90	(4.19)	26.57	(5.28)
Median	25.60		23.99		24.44	
Min/max	21.10	41.35	18.90	33.61	18.90	41.35
Enhancement (HU)						
Mean (SD)	280.90	(50.84)	258.60	(39.28)	269.75	(46.06)
Median	269.51		260.35		266.60	
Min/max	184.79	369.24	205.74	335.74	184.79	369.24
Region of interest (cm^3)						
Mean (SD)	0.43	(0.16)	0.54	(0.35)	0.49	0.27
Median	0.41		0.41		0.41	
Min/max	0.20	0.72	0.22	1.39	0.20	1.39

of a 5-point scale (1: Bad, no diagnosis possible; 2: Poor, diagnostic confidence significantly reduced; 3: Moderate, but sufficient for diagnosis; 4: Good; 5: Excellent). In an attempt to eliminate subjective bias, the scoring was performed double blinded so neither the radiologists, nor the patients knew which scanning protocol was being used.

Difference in image quality of the CTA studies in patients with abdominal aortic aneurysm was compared with the others in each group.

2.6. Statistical analysis

We performed a power calculation on the ROI sample size and number of patients. The power calculation on the ROI sample size, which for each protocol is 450 (30 ROI's times 15 patients), assuming $\alpha = 0.05$ and a difference in mean attenuation value of 27 HU between the two protocols with a standard deviation of 51, can achieve a power of approximately 100%. However, because these measurements are not independent a power calculation on patient base is more appropriate.

The power of this pilot study, calculated with a sample size of 15 patients and a significance level of 0.05, is 43% (1 sided test). This result indicates that further validation is required within a larger study population.

To determine if the difference between the mean attenuation values for both protocols was significant the Student's *t* test was used.

The uniformity, important for this research, is the uniformity in the craniocaudal direction of the abdominal aorta and iliac arteries. By computing the difference in trend lines for each patient and both groups the uniformity of both protocols can be calculated. Student's *t* test was used to determine the significant difference between both protocols.

To analyze the qualitative assessment of the three radiologists, the score per patient and per protocol were averaged. The Mann–Whitney (two-tailed) test was used to determine if the difference between the two protocols was significant. The interobserver agreement between the assessments of the three radiologists was calculated using the Cohen's Kappa (κ) statistics. Agreement was classified as 'very good' (κ values > 0.8), 'good' ($\kappa = 0.61–0.8$), 'moderate' ($\kappa = 0.41–0.6$), 'fair' ($\kappa = 0.21–0.4$) or 'poor' ($\kappa \leq 0.2$) [12]. Statistical analysis was performed using SPSS 19.0 software (SPSS Inc., Chicago, USA). To determine if the differences between both protocols was significant, a value of $p \leq 0.05$ (double side) was considered statistically significant. Normality of the data distribution was tested before using the Student's *t* test for comparison.

3. Results

In total 30 patients referred for CTA of the abdominal aorta were enrolled in this trial. The baseline characteristics of the study population were mostly balanced between both groups (Table 2).

Between both groups the presence of a metallic stent, calcifications and/or an aneurysm was distributed as follows; 4 patients of protocol I and 5 patients of protocol II contained a metallic stent, all 15 patients of each protocol contained calcifications. An aneurysm was present in 6 patients of protocol I and 8 patients of protocol II. The difference in intravascular enhancement in patients with an aneurysm compared with patients without an aneurysm was not significant in both groups ($p = 0.153$ and $p = 0.234$, respectively). The difference in image quality in patients with an aneurysm compared with patients without an aneurysm was not significant in both groups ($p = 0.083$ and $p = 0.787$, respectively).

3.1. Quantitative analysis

The mean attenuation of the first protocol showed a higher overall vascular enhancement compared to the second protocol, with an average mean contrast enhancement value of 280.90 ± 50.84 HU (standard deviation) and 258.60 ± 39.28 HU respectively (Fig. 1).

The mean attenuation values of the main abdominal arteries arising from the aorta are represented in Table 3.

The observed *t* statistics for the mean attenuation for both protocols is 1.344 with a confidence interval of 95% between −11.68 and 56.28 ($p = 0.190$).

Table 3
Results of the mean attenuation values from the main arteries arising from the abdominal aorta. The mean attenuation value in HU of a single ROI was measured 3 times at 5 different positions in the celiac trunk, renal arteries, and superior and inferior mesenteric arteries.

	Protocol I				Protocol II			
	Mean	Min	Max	SD	Mean	Min	Max	SD
Celiac trunk	252.98	185.86	306.83	29.26	251.83	189.01	299.91	28.64
Superior mesenteric artery	267.66	202.17	315.36	25.61	263.34	209.67	301.00	22.14
Left renal artery	234.61	168.35	291.49	29.65	234.39	151.50	295.48	37.26
Right renal artery	242.22	167.20	297.14	32.92	232.86	150.83	288.25	34.84
Inferior mesenteric artery	219.63	152.81	279.53	38.17	192.01	96.17	265.50	50.01

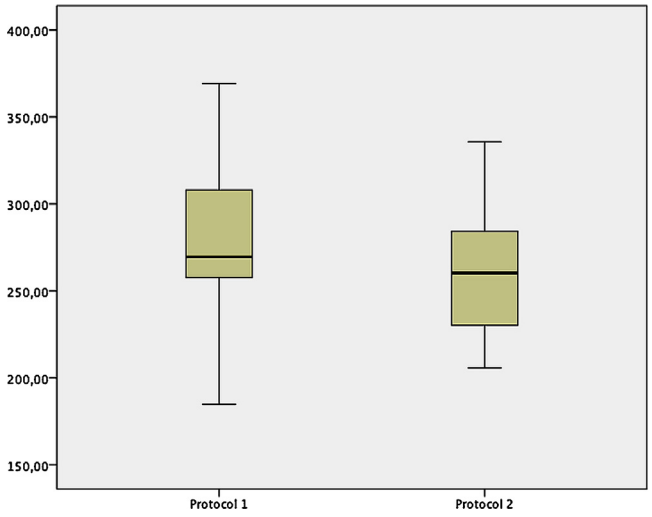

Fig. 1. Comparison of mean attenuation values between both groups. Protocol I shows a mean attenuation value of 280.90 ± 50.84 HU (standard deviation). Protocol II shows a mean attenuation value of 258.60 ± 39.28 HU.

To compare the two injection protocols, the attenuation of contrast enhancement was averaged for both protocols. The results are shown in Fig. 2, where the *x*-axis shows the measurements of the 30 ROI's in the aorta from the celiac trunk to the iliac arteries. In protocol I a lower attenuation decrease from cranial to caudal in the abdominal aorta occurred than in protocol II, which however did not reach statistical significance ($p = 0.107$).

3.2. Qualitative analysis

The results of the qualitative assessment are represented in Table 4. The scoring of the three radiologists is averaged per protocol. The mean image quality of protocol I was rated 4.31 (range: 3.67–5.00) and of protocol II 4.11 (range: 2.67–5.00) on a 5-point scale (Figs. 3 and 4) ($p = 0.499$).

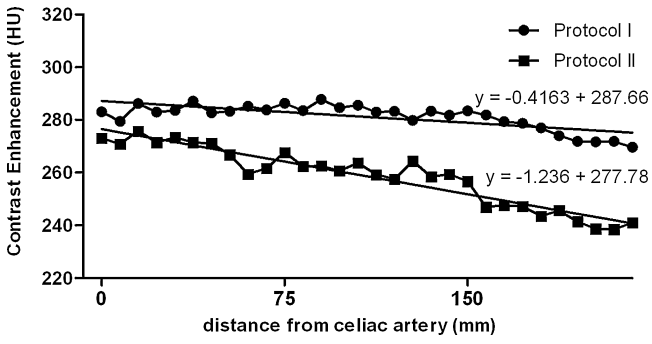

Fig. 2. Mean variability in contrast enhancement of both injection protocols, where the variability in the attenuation is presented along the *y*-axis. The *x*-axis shows the measurements in the abdominal aorta from cranial to caudal. A trend line was used to demonstrate the uniformity of the enhancement along the *x*-axis.

Table 4
Results of the qualitative assessment of the vascular enhancement performed by three experienced radiologists. Image quality was assessed with the use of a 5-point scale (1. Bad, no diagnosis possible; 2. Poor, diagnostic confidence significantly reduced; 3. Moderate, but sufficient for diagnosis; 4. Good and 5. Excellent). The scoring is averaged per protocol.

	Protocol I		Protocol II	
Mean	4.31		4.10	
SD	0.46		0.65	
Median	4.33		4.33	
Min/max	3.67	5.00	2.67	5.00

The Cohen's Kappa shows a 'fair' agreement (of $\kappa = 0.2981$) between the assessments of the radiologists.

4. Discussion

This study showed that with an evident decreased contrast medium volume (50 mL Optiray 350) still a qualitatively and adequate enhancement in abdominal CTA can be realized. With regard to the diagnostic performance and image quality of the abdominal aorta a test bolus injection protocol realized a reduction of 44%, compared to the multiphasic injection protocol (89 mL Optiray 350), with no significant difference observed between the two protocols. Compared to a customary CTA scan protocol with 100 mL contrast media this is a reduction of 50%.

The result of the quantitative analysis shows that there is a small difference between the uniformity of both protocols, which is however too small to be significant (Fig. 2). The difference within the group could be caused by factors which influence the transport of contrast medium along the blood vessels, for example the cardiac output, age, gender, weight, but also the presence of a metallic stent, calcifications or an aneurysm [10]. The most important factor might be the presence of an aneurysm. In an aneurysm the lumen volume may increase abruptly, which causes a dilution of contrast media (i.e., a decrease in enhancement). To diminish the influence of the various factors, patients were randomly assigned into the two groups. The quantitative analysis shows that with the multiphasic injection (protocol I), the enhancement is higher as compared to the test bolus injection protocol (protocol II) (Fig. 1). The overall higher enhancement in protocol I can be explained by the fact that more contrast medium is used.

This study confirmed the findings of a recent CTA study [10], which demonstrated that enhancement patterns of the multiphasic injection protocol was quantitatively as well as qualitatively comparable to the uniphasic injection protocol, using 89 mL and 100 mL of contrast medium respectively. The multiphasic injection protocol achieved a better uniform and prolonged contrast enhancement.

The basic premise of the multiphasic injection technique (protocol I) is that uniform vascular enhancement occurs when contrast material accumulation achieves a steady state in vessels. This can be achieved when the contrast medium administered into the central

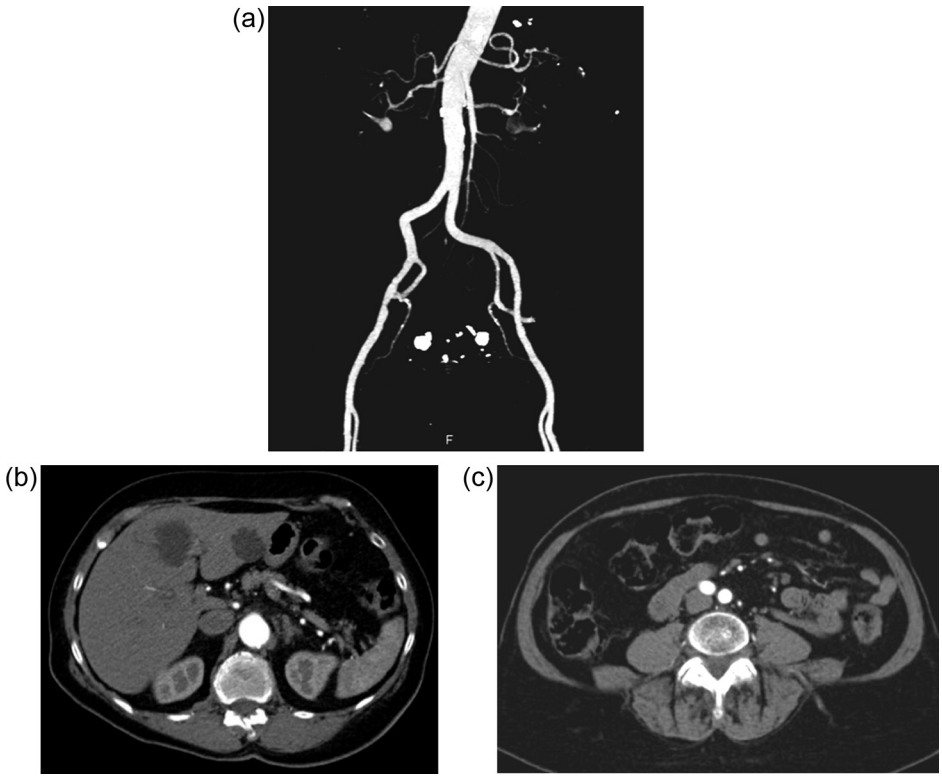

Fig. 3. Coronal CT image (a) maximum injection projection of the aorta abdominals and axial CT images at the level of the renal artery (b) and of the iliac arteries (c). The CT images were obtained using a multiphasic injection technique, with 89 mL of contrast medium in a 59 year-old man (BMI: 24.8). The quantitative assessment of the mean aortic enhancement is 298.52 HU and the qualitative assessment score is 5 (i.e., excellent).

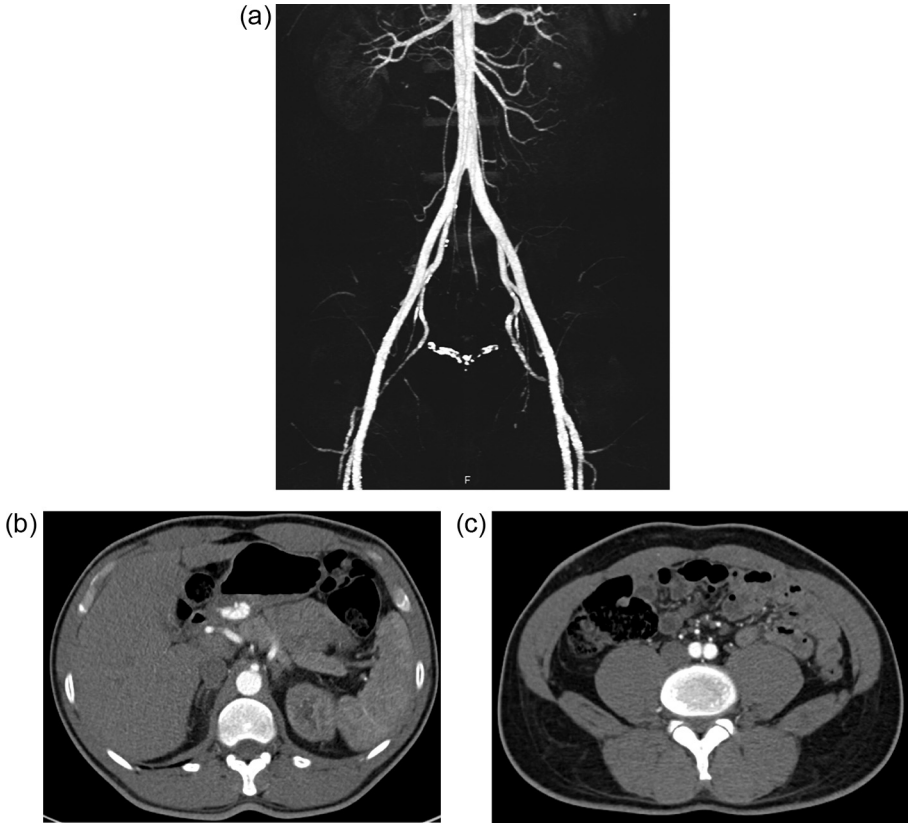

Fig. 4. Coronal CT image (a) maximum injection projection of the aorta abdominals and axial CT images at the level of the renal artery (b) and at the iliac arteries (c). The CT images were obtained using a test bolus injection technique, with 50 mL of contrast medium in a 39 man year-old man (BMI: 23.4). The quantitative assessment of the mean aortic enhancement is 323.19 HU and the qualitative assessment score is 5 (i.e., excellent).

blood compartment, delivered with an exponentially decreasing rate, is balanced by the rate of contrast medium clearance from the same compartment [13]. The injection bolus profile of this method was derived from a physiologically based pharmacokinetic model. According to this prediction model, a multiphasic-rate injection bolus with exponentially decreasing rate (e.g., $4e^{(-0.01t)}$ mL/s, where t is time) provides a uniform vascular enhancement [14]. Bea et al. [15] compared several exponential decay coefficients in simulation and found a decay of 0.01 mL/s to be appropriate in humans. This decay is the ratio of the cardiac output to the systemic distribution volume of contrast medium in an average-size adult human.

With fast MDCT, the use of the contrast material arrival time as a scan delay may result in scanning too early. Therefore, the scan delay should be calculated as the sum of contrast material arrival time plus an additional delay, also called diagnostic delay, such that the diagnostic CT scan is adequately delayed and centred at the maximum of contrast enhancement [14]. In our study the diagnostic delay was set on 8 s.

There were several limitations in this study. First, CTA scans of the abdominal aorta were performed using 120 kV Recently, various techniques and patient-based strategies have focused on reducing the radiation dose delivered during CT studies [16–19]. Low tube voltage CTA of the body with 100 kV or 80 kV represents the most commonly applied technique for radiation dose and contrast medium volume reduction, with savings ranging from 20% to 50% when compared to the conventional protocol employing 120 kV [17,20].

Second, raw data-based iterative reconstructions also has the potential to reduce the radiation dose more than 50% as compared to a standard reconstruction with filtered back projection, while maintaining diagnostic image quality [21,22].

Third, the scan delay was not determined using the proposed empirical scheme for determining the scan delay by Bae et al. [14], where the scan delay (T_{DELAY}) is calculated to be equal to the estimated peak enhancement time (T_{PEAK}) minus half the scan duration (T_{SD}): $T_{DELAY} = T_{PEAK} - (1/2)T_{SD}$. The time to peak enhancement of the test bolus, which is related to the circulation time, helps adjust for individual variations in acquisition timing [23]. With fast MDCT, the use of the contrast material arrival time as a scan delay may result in scanning too early. Therefore, the scan delay should be calculated as the sum of contrast material arrival time plus an additional delay, also called diagnostic delay [14], such that the diagnostic CT scan with full bolus injection of 40 mL is adequately delayed and centred at the maximum of contrast enhancement. In this study the diagnostic delay was set on 8 s, 5 s of test bolus plus an additional 3 s as reserve for not scanning too early.

5. Conclusion

This study showed that by using a test bolus injection and the administration of 50 mL of contrast medium overall, CTA of the abdominal aorta can effectively be performed, with regard to quantitative and qualitative adequate vessel enhancement. Due to the relatively small sample size validation with a larger study population is required. However, the findings of this study justifies additional research to the lower limits of the iodine load needed and contrast medium volumes used in CTA. An additional decrease of the amount of contrast material used may be achieved by scanning with low voltage (80 kV).

Conflict of interest

No conflicts to declare.

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