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Reduced contrast medium in abdominal aorta CTA using a multiphasic injection technique

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ABSTRACT

Purpose: The purpose of this study was to determine if with a multiphasic injection technique the administered amount of contrast medium for abdominal computerized tomographic angiography (CTA) can be decreased, whilst improving CT image quality.
Materials and methods: In 30 patients a multiphasic injection method was compared to the standard uniphasic contrast medium injection protocol. Fifteen patients underwent abdominal CTA with a standard uniphasic injection protocol (protocol I) receiving 100 mL of a non-ionic radiopaque contrast agent (Ioversol). The second group of 15 patients underwent CTA with a multiphasic injection protocol (protocol II) receiving a total of 89 mL Ioversol. Vascular contrast enhancement and difference in enhancement uniformity were assessed quantitatively and image quality was assessed by three independent radiologists.
Results: Quantitative assessment of the vascular contrast enhancement showed that there was no significant difference in enhancement uniformity for patients between the protocols. The image quality was rated as being good to excellent in 81.8% and 88.0% of the scans, for protocol I and protocol II, respectively. However these differences were not statistically significant.
Conclusion: By using a multiphasic injection technique with CTA of the abdominal aorta a reduction of 11 percent of contrast medium can be realized. Enhancement patterns are quantitatively as well as qualitatively comparable to the standard contrast medium injection protocol.

1. Introduction

The standard imaging method for the evaluation of the anatomy of major vessels, such as the aorta, is computerized tomographic angiography (CTA) [1]. The injection technique used with CTA is a uniphasic method in which contrast medium is injected at a constant rate during the entire injection in order to achieve sufficient vascular enhancement. This injection technique results in a steadily rising vascular contrast enhancement profile with a single peak of enhancement occurring shortly after completion of the injection. Hence, the vascular enhancement is not uniform throughout the entire image acquisition [2]. Non-uniform enhancement can result in artefactual findings, such as filling defects and perceived stenoses [3].

A method of injecting contrast medium that facilitates uniform vascular enhancement for the duration of the image acquisition is highly desirable in CTA [4]. Experimental studies have demonstrated that this can be achieved with multiphasic contrast injection [1]. An additional advantage is that the amount of intravenous contrast medium can be decreased, which may reduce the incidence of contrast-induced nephropathy.

The decelerating or multiphasic contrast medium injection can easily be performed with the nowadays commercially available contrast medium injectors.

The purpose of this study is to reduce the administered contrast medium volume in abdominal CTA with 11 percent by using a multiphasic injection technique, whilst improving image quality.

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2. Materials and methods

2.1. Study design

A randomized, double blind feasibility study in patients referred for CTA of the abdominal aorta was performed. The study protocol was approved by the institutional 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 thirty patients who met the inclusion and exclusion criteria (Table 1) were included. All patients participating in this study were weighed and their heights were noted. After providing written informed consent, patients were randomized into two different injection protocol groups. Fifteen patients were scanned according to the uniphasic or constant rate injection protocol (protocol I) and received 100 mL of Ioversol i.e., Optiray 350 (350 mg of iodine per mL, Mallinckrodt Medical B.V., Petten, The Netherlands). Fifteen patients were assigned to the multiphasic or exponentially decelerated injection protocol (protocol II), resulting in the administration of a reduced amount of 89 mL of Ioversol.

Injection of the contrast medium was immediately followed in both protocols by a Bolus of 20 mL NaCl. 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 artery.

2.2. Constant rate or uniphasic injection (protocol I)

Patients in the protocol I group were injected according to the uniphasic method. The contrast medium used was 100 mL of Ioversol, which was injected at a constant rate of 4 mL/s for 25 s via an 18-gauge intravenous catheter. All patients were injected in the medial cubital vein at the elbow. The contrast medium was injected using a dual head contrast delivery injector (OptiVantage™ Injecton System, Tyco Healthcare Mallinckrodt, St. Louis, United States).

2.3. Exponentially decelerated or multiphasic injection (protocol II)

Patients in this group were injected using an exponentially decelerating (multiphasic) rate. Bae et al. [1] compared several exponential decay coefficients in simulations 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 volume of distribution of contrast medium in an average-size adult human. Ioversol was injected for 25 s with a starting injection rate of 4 mL/s, which decelerated exponentially with a decay of 0.01 mL/s. The end injection rate can be calculated using the following formula:

$$V(t) = 4 \cdot e^{(-0.01)t} \rightarrow 4 \cdot e^{(-0.01)25} = 3.1 \quad (1)$$

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

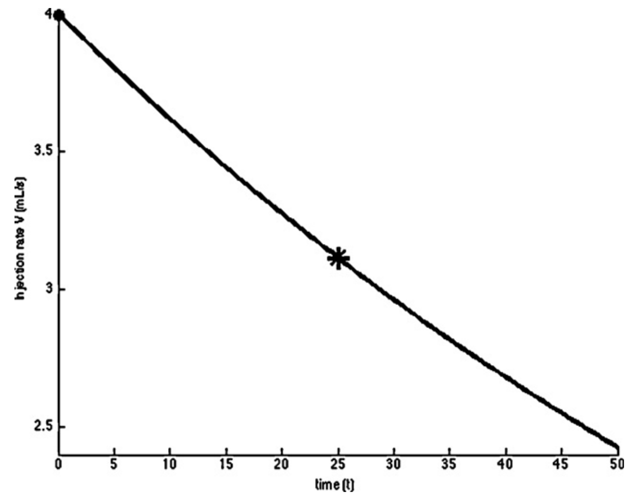

Fig. 1. Shows the exponentially decelerating (multiphasic) rate of injection protocol II. The injection started at $t = 0$ with an injection rate of 4 mL/s (dot) and ended at $t = 25$ with an injection rate of 3.1 mL/s (asterisk).

where t is the time in s. After 25 s the injection rate is 3.1 mL/s (Fig. 1). When integrating formula (1) over time, the total injected volume can be determined:

$$\int_{t=0}^{t=25} 4 \cdot e^{(-0.01)t} dt = [-400 \cdot e^{(-0.01)t}]_{t=0}^{t=25} = 88.5 \sim 89 \quad (2)$$

Upon completion of the 25 s injection with the multiphasic method, a total amount of 89 mL contrast medium was injected. All patients were injected in the medial cubital vein at the elbow. The decelerating injection was performed by the dual head injector of Tyco Healthcare Mallinckrodt, using the Timing Bolus™ Feature software.

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 as follows: rotation time, 0.33 s; beam collimation, 128 mm × 0.6 mm; reconstruction section thickness, 3 mm; tube voltage, 120 kV; helical pitch, 1.2; table speed, 28 cm/s; mean total DLP, 533 mGycm; mean effective dose, 7.9 mSv; ref. output, 148 mAs. Both groups were scanned with the same CT settings.

3. Assessment of vascular enhancement

3.1. 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 region of interest (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. 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 (Syngo.Via, 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.

3.2. Qualitative assessment

Qualitative assessment of the vascular enhancement was performed by three experienced radiologists, who were unaware of each other's findings. They scored the images visually with respect to diagnostic usefulness and interpretability 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). 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.

3.3. Statistical analysis

Statistical analysis was performed using SPSS 19.0 software (SPSS Inc., Chicago, USA).

To determine if the difference between the mean attenuation values for both protocols was significant 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. Student's *t*-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' ($\kappa \leq 0.2$).

For all statistical determinations a value of $p \leq 0.05$ (double side) was considered statistically significant.

4. 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). However, in group II one patient was weighing 30 kg, which is certainly not considered as an average sized human adult. As a consequence BMI of 11.40 is also not in the normal range of a human adult. Between both groups the presence of a metallic stent, calcifications and/or an aneurysm was equally distributed. Each group of 15 patients contains metallic stents in 3 patients, calcifications in 14 patients and aortic aneurysms in 8 patients.

4.1. Quantitative analysis

The mean attenuation of the first protocol showed a higher overall vascular enhancement compared to the second protocol, with a mean attenuation value of 300.74 HU ± 35.22 (standard deviation) and 273.93 HU ± 67.80, respectively (Fig. 2).

To compare the two injection techniques, the attenuation of the enhancement was averaged for both protocols. The results are shown in Fig. 3, where the *x*-axis shows the measurements in the aorta from cranial to caudal. A trend line was used to demonstrate the uniformity of the enhancement along the *x*-axis. The trend line in Fig. 3 of protocol II shows a lower attenuation decrease from cranial to caudal in the abdominal aorta than in protocol I. This means that in protocol II the attenuation is through out the vascular structures more uniform.

4.2. Qualitative analysis

The results of the qualitative analysis are represented in Table 3. The scoring of the three radiologists is averaged per protocol.

The image quality was rated as being 'good' to 'excellent' in 81.8% and 88.0% of the scans, for protocol I (Fig. 4) and protocol II (Fig. 5), respectively.

Table 2
Demographic data of the study population.

	Protocol I ($n = 15$)		Protocol II ($n = 15$)		All ($n = 30$)	
Gender						
Male	10	(66.66%)	10	(66.66%)	20	(66.66%)
Female	5	(33.33%)	5	(33.33%)	10	(33.33%)
Age (years)						
Mean (SD)	71.93	(7.85)	66.93	(10.05)	69.43	(9.22)
Median	70.00		67.00		68.00	
Min/max	59.00	85.00	47.00	82.00	47.00	85.00
Height (cm)						
Mean (SD)	170.06	(8.40)	174.60	(8.12)	172.33	(8.44)
Median	170.00		175.00		172.00	
Min/max	157.00	185.00	160.00	185.00	157.00	185.00
Weight (kg)						
Mean (SD)	77.53	(12.57)	77.20	(18.33)	77.36	(15.44)
Median	77.00		83.00		78.50	
Min/max	58.00	98.00	30.00	100.00	30.00	100.00
Body mass index (kg/m^2)						
Mean (SD)	26.88	(4.60)	25.00	(4.59)	25.94	(4.62)
Median	25.70		25.40		25.50	
Min/max	20.50	33.90	11.40	30.40	11.40	33.90
Enhancement (HU)						
Mean (SD)	300.74	(35.22)	273.93	(67.80)	288.00	(54.13)
Median	300.43		271.30		285.32	
Min/max	234.53	357.54	185.86	465.01	185.86	465.01
Region of interest (cm^3)						
Mean (SD)	1.1	(0.56)	1.8	(1.47)	1.44	(1.15)
Median	0.9		1.2		1.1	
Min/max	0.6	2.3	0.5	5.5	0.5	5.5

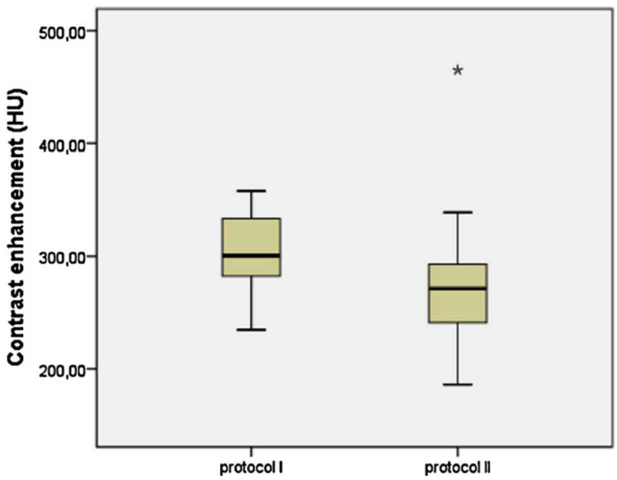

Fig. 2. Box plot demonstrating the comparison of the mean attenuation values between both scan protocol groups. Protocol I had a mean attenuation value of 300.74 HU ± 35.22. Protocol II had a mean attenuation value of 273.93 HU ± 67.80. The asterisk in the plot of protocol II can be explained by the fact that this patient had a very low BMI of 11.4, which resulted in a higher attenuation value.

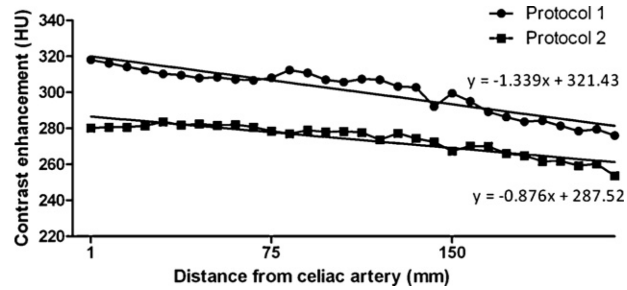

Fig. 3. Mean variability in contrast enhancement of both injection protocols. The attenuation variability is presented along the *y*-axis. The *x*-axis shows the HU (enhancement) measurements in the abdominal aorta from cranial to caudal. A trend line demonstrates the uniformity of the enhancement along the *x*-axis.

4.3. Statistical analysis

The observed t statistic for the mean attenuation values for both protocols is 1.304 with a confidence interval of 95% between −14.53 and 65.49 ($p = 0.203$).

For the uniformity of the two protocols, the t statistic is −1.219 with a confidence interval of 95% between −0.72 and 1.64 ($p = 0.233$).

Fig. 4. Coronal CT image (a), maximum injection projection of the abdominal aorta and axial CT images at the level of the renal artery (b) and the iliac arteries (c). The CT images were obtained using a uniphasic injection technique, with 100 mL of contrast medium in a 67-year-old man (BMI: 24.2). The quantitative assessment of the mean aortic enhancement is 234.54 HU and the qualitative assessment score is 5 (i.e., excellent).

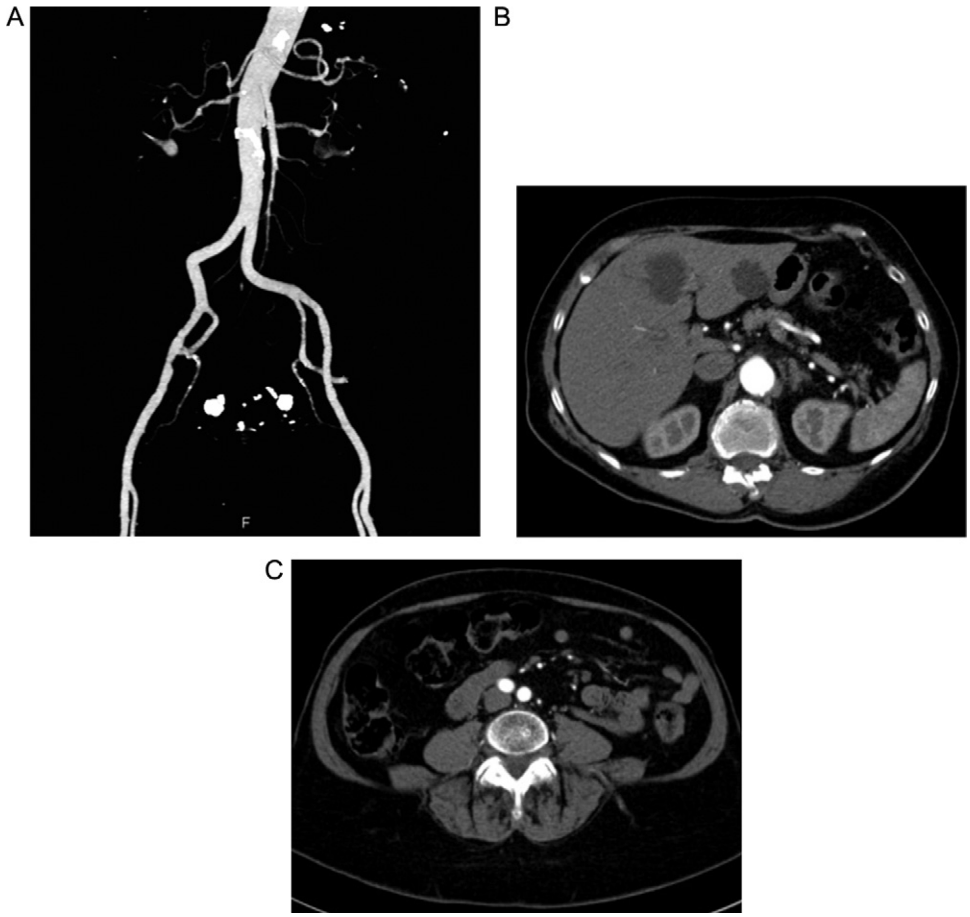

Fig. 5. Coronal CT image (a), maximum injection projection of the abdominal aorta and axial CT images at the level of the renal artery (b) and the iliac arteries (c). The CT images were obtained using a multiphasic injection technique, with 89 mL of contrast medium in a 59-year-old man (BMI: 24.8). The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

Table 3
Results of the qualitative assessment of the vascular enhancement performed by three experienced radiologists. They scored the images visually with respect to diagnostic usefulness and interpretability 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).

	Protocol I		Protocol II	
Mean (%)	4.08	(81.78)	4.40	(88.02)
SD	0.82		0.55	
Median	4.00		4.67	
Min/max	2.33	5.00	3.00	5.00

The t statistic for the qualitative assessment of the radiologist is −0.669 with a confidence interval of 95% between 0.21 and −0.83 (p = 0.512). The Cohen's Kappa shows a 'moderate' agreement (of κ = 0.41) between the radiologists.

For all the observed t statistics the mean variability between the two protocols showed no statistically significant difference.

5. Discussion

This study showed that, with regard to diagnostic performance and image quality in CTA of the abdominal aorta, a lower contrast medium volume of 89 mL of Ioversol (350 mg/mL iodine) using a multiphasic injection protocol was comparable to 100 mL of Ioversol (350 mg/mL iodine) using a standard uniphasic injection protocol. The exponential decelerating rate of the multiphasic injection protocol can actually be considered as linear, because the duration of the injection is still in the linear region of formula (1) (Fig. 1).

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. 3). 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. 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 uniphasic injection (protocol I), the enhancement is higher as compared to the multiphasic injection technique (protocol II). The overall higher enhancement in protocol I can be explained by the fact that more contrast medium is used.

Post processing, for example for three-dimensional images, is frequently based on a threshold value of the CT attenuation [4]. To achieve uniform enhancement it is crucial to reach a steady-state plasma concentration of iodinated contrast medium during acquisition for perfused blood volume CT [5,6].

Bae et al. [1] conducted a study in 2000, comparing the uniphasic injection with a bi- and multiphasic exponential decay injection method with the use of a computer-based compartmental model and a porcine model. This study shows that the computer simulation corresponds with the experimental results of the porcine model that a multiphasic injection achieves better uniform prolonged enhancement. The principle behind this technique is that uniform vascular enhancement occurs when contrast material accumulation achieves a steady state in vessels. This state can be achieved when the contrast medium administered into the central blood compartment, delivered with an exponentially decreasing rate, is balanced by the rate of contrast medium clearance from the same compartment [2].

In 2004 Bae et al. [2] confirmed his findings of previous studies in a clinical study. In our clinical study we showed that with less contrast medium still a qualitatively adequate enhancement can be realized. In contrast to the study of Bae we inject during a shorter time period. Bae injected during 40 s and used a total amount of 134 mL iodinated contrast medium. Bea predicted that shortening of scan time would result in a poorer enhancement, however we proved the contrary.

Uniform enhancement can also contribute to a more efficient use of contrast medium [4]. With a given contrast medium volume, uniform contrast enhancement with a magnitude of peak enhancement lower than that in a non-uniform contrast enhancement profile would provide a longer temporal window of adequate vascular enhancement and thereby result in a longer optimal scanning interval [2]. Theoretical and animal study results have demonstrated that an exponentially decelerated, or multiphasic, injection method can facilitate uniform and prolonged vascular contrast enhancement in CT angiography and thereby potentially improve image quality and efficiency of contrast medium use [1].

A patient's body weight and the amount of contrast medium injected are closely related to the degree of contrast enhancement. Research performed by Bae [7] showed that the mean aortic attenuation is significantly higher in patients with a low BMI. Therefore, the asterisk in Fig. 2 can be explained by the fact that this patient had a very low BMI of 11.4, which resulted in a higher attenuation value.

Contrast-induced nephropathy (CIN) is a well-recognized complication of radiographic contrast administration and is the third leading cause of hospital-acquired renal insufficiency [8]. 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 [9]. CIN leads to prolonged hospitalization, dialysis and increased mortality [10].

Further research should be initiated to investigate if a larger reduction of contrast medium can be realized whilst maintaining clinically usable image quality.

6. Conclusion

This study showed that enhancement patterns of a standard uniphasic injection protocol and a multiphasic injection protocol are 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.

Acknowledgements

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