Low-dose multidetector-row CT angiography in the evaluation of infrarenal aorta and peripheral arterial occlusive disease

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Purpose

Peripheral vascular occlusive disease (PAOD) is a chronic and progressive major health problem with a reported prevalence of 4.5% to 10% in people up to 65 years of age, increasing to 20% in men and women older than 75 years [1-2].

CT angiography (CTA) of aortoiliac and lower extremity arteries is a relatively new application of CT imaging that has developed after the introduction of multidetector row scanners [3-4]. Multi-detector row CT (MDCT) is able to noninvasively image lower extremity inflow and run-off from the abdominal aorta to the feet with a single injection of contrast material and a single acquisition of less than 15-second duration by using a 64-row MDCT scan, with an adequate spatial resolution. MDCT angiography is faster, less costly and less invasive with fewer potential complications, even if the most important disadvantage of CT is represented by the use of ionizing radiation.

We know that CT scans performed with a low dose reduce the signal to noise ratio of the images with a subsequent decrease in image quality.

The purpose of our study was to investigate the possibility of reducing X-ray exposure during 64-row spiral computed tomography (MDCT) angiography and to define the real influence of radiation dose on diagnostic accuracy of CT in the evaluation of infrarenal aorta and peripheral arterial occlusive disease.
Methods and Materials

Study design

This study is a unicenter, blinded, randomized, comparison of 3 different X-ray exposure CT-acquisition protocols.

All imaging performed in this study were part of the routine diagnostic assessment of patients with infrarenal aorta and peripheral arterial occlusive disease at our institution and were considered an acceptable part of patient care. The ethical conduct of the study was approved by our departmental review board and was performed in agreement with the 1990 Declaration of Helsinki and subsequent amendments. Each patient provided informed consent prior CT examination.

Any patient with PAOD clinically assessed and confirmed by color Duplex Ultrasonography who underwent our department to be studied with MDCT were evaluated for the enrolment in our study.

In detail, all patients were firstly scheduled on the basis of the body mass index (BMI = weight in kilograms divided by the square of the height (m) into one of the following categories: category 1: BMI < 18.5 kg/m2 (underweight patients); category 2: BMI between 18.5 and 24.9 kg/m2 (normal patients); category 3: BMI between 25 and 29.9 kg/m2 (overweight patients); category 4: BMI > 30 kg/m2 (obese patients). Patients with a BMI>30 kg/m2 (obese patients) were excluded from the study.

Also excluded were patients with history of congestive heart failure, previous myocardial infarction or severe rhythm disturbances as well as patients with severe renal impairment or serum creatinine levels greater than 2 mg/dl and patients with any medical conditions or circumstances which would significantly decrease the chances of obtaining reliable data or achieving the study objectives (psychiatric disorders, drug dependency, dementia).

The enrolled patients were randomized into one of the three X-ray exposure acquisition protocols (20 patients/group), in accordance with a predetermined randomization schedule.

MDCTA Examinations

CT angiography was performed with 64-row CT Lightspeed VCT scanner (GE Medical Systems). Patients were in the supine position with their feet first. After acquisition of non-contrast CT scans from the diaphragm to the symphysis pubis, MDCT angiography was performed from 2 cm above the origin of renal arteries to the ankle. All studies were performed in the cranio-caudal direction with the following parameters: 0.625x64mm
collimation, 0.7-second gantry rotation, pitch 0.9; scan duration ranged between 18 and 25 seconds.

Contrast-enhanced images were obtained during intravenous injection of 100 ml of iodinated non-ionic contrast medium (Iomeprol 400mgI/mL, Iomeron; Bracco, Milan, Italy) + 40mL of saline solution, at a flow rate of 4 ml/s via an antecubital vein. Arterial phase acquisition were performed from suprarenal abdominal aorta to the ankle. Scan delay were individualized per patient, using GE’s proprietary bolus-tracking software (SmartPrep), to capture 150 HU on the abdominal aorta, at the level of the celiac trunk, to trigger scanning and ensure a correct peak enhancement, by adding a diagnostic delay of 8 seconds.

Safety and tolerability of both contrast agents were assessed by recording the occurrence of adverse events as well as heat sensation or pain at the site of injection.

All patients were randomized into one of the three X-ray exposure acquisition protocols, as follow: GROUP A (standard-dose): Noise index: 26 (SMARTmA); 120 KV; GROUP B (low-dose): Noise index: 26 (SMARTmA); 80 KV; GROUP C (ultra-low-dose): Noise index: 30 (SMARTmA); 80 KV.

Smart mA system is an automatic exposure control which combines both z-axis and angular tube current modulation to adjust the dose to the size and shape of individual patients. Prior to scanning, the user selects the desired image quality, or noise index. Based on a single scout scan, the system adjusts the exposure during the CT scan to achieve that level of acceptable noise across the region of interest. The system increases and decreases the mA as it encounters various anatomy thicknesses and asymmetries. A lower noise index is associated to an higher mAs provided by scanner, and, consequently, to an higher radiation dose.

**Image Analysis**

All CT images were reviewed in random order on a computer dedicated workstation by two experienced radiologists (RM and MS with 12 and 6 years of experience in vascular CT, respectively) in consensus for quantitative and qualitative evaluation and in a blinded independently fashion for diagnostic performance. Three-dimensional reconstructions were interactively performed directly by the two readers who could choose different planes and reconstruction algorithms provided by the workstation, generating any plane or perspective best suited for interpretation.

To minimize learning bias, names, ages, and identification numbers of patients, and imaging parameters will be always hidden during the review. The specific image sets will be randomly selected by another author (RD with 3 years of experience in body CT), not involved in the review.
Image evaluation was performed first in terms of the diagnostic quality of the images. For this assessment, the two readers in consensus assessed the technical adequacy of the examinations (technically adequate for diagnosis or technically inadequate; non-diagnostic) and the presence/absence of artifacts (1 = none, 2 = minimal, not compromising image evaluation, 3 = substantial, compromising image evaluation).

Evaluation of all technically adequate image sets, without artifacts compromising image evaluation, was thereafter performed in terms of both quantitative and qualitative arterial phase enhancement. Quantitative evaluation was only performed on axial images whereas qualitative assessment was performed on both axial and 3D-images.

The two assessments were performed in two different reading sessions separated by an interval of 1 month.

**Image noise**

As dose reduction is responsible for noise in the CT image, an objective and subjective assessment of noise was performed. The objective assessment of noise was obtained by measuring the standard deviation of pixel values in a homogeneous region at two anatomical levels, namely the abdominal aortic lumen above the celiac trunk origin and the gastric cavity, by placing a circular region of interest (ROI) with an area ranging from 0.5 and 0.6 cm\(^2\). The subjective assessment, defined by the grainy appearance of the CT images, was visually performed on both axial and 3D images by using a five-point scale, as follows: a score of 1, for minimum or no image noise; 2, for less-than-average noise; 3, for average noise in an acceptable image; 4, for above-average increased noise; 5, for unacceptable noise.

**Image quality**

All technically adequate images were evaluated for quantitative and qualitative contrast enhancement.

The maximum enhancement in HU was made at the following sites: proximal aorta (2 cm above the renal arteries), distal aorta (2 cm above the aortic carrefour), right and left iliac common iliac arteries, right and left common femoral arteries, right and left superficial femoral arteries, right and left popliteal arteries and right and left leg (at midcalf).

In order to calculate contrast-to-noise ratios (CNR) (difference between aortic lumen and psoas muscle/ deviation standard of psoas muscle) mean enhancement value as well as deviation standard of psoas muscle were measured.
The maximum enhancement in HU was determined by placing a circular region-of-interest (ROI) within the center of the vessel. The ROI was made as large as possible, according to the vessel size; wall calcification or metallic artifact related to vascular stents were avoided.

Both axial and 3D images were also separately re-assessed in terms of qualitative contrast enhancement on different vascular segments: a) aorto-iliac district; b) femoropopliteal district; c) infrapopliteal district: d) foot.

Subjective evaluation of image quality was assessed in order to visually define differences between the different protocols. A four-point scale were used to score image quality as follows: 1, non diagnostic quality (poor diagnostic information, impossible to detect or exclude vascular lesions, with beam-hardening artifacts affecting image interpretation); 2, moderate diagnostic quality (inhomogeneous enhancement in vessel lumen, evaluation of vascular lesions possible with low diagnostic confidence, with beam-hardening artifacts not affecting image interpretation); 3, good visualization (good and almost completely homogeneous enhancement in vessel lumen, evaluation of vascular lesions possible with satisfactory diagnostic confidence, without beam-hardening artifacts); 4, excellent visualization (optimal and completely homogeneous enhancement in vessel lumen, evaluation of vascular lesions possible with high diagnostic confidence, without beam-hardening artifacts).

**Radiation Dose Estimation**

The weighted CT dose index (CTDIw), expressed in milligrays (mGy) was used to calculate the CT radiation dose reveived by patients. The CTDIw was estimated from the values of beam collimation, kilovolts and effective mAs.

Dose reduction was expressed as the percentage obtained by dividing the effective dose of the standard protocol examination (Noise index: 26 SMARTmA/120 KV) by the effective dose of the low-dose (Noise index: 26 SMARTmA/80 KV) and ultralow-dose (Noise index: 30 SMARTmA/80 KV) protocol, respectively.

**Statistical Analysis**

The study was designed as a calibrated phase II clinical trial.

This design consisted of random allocation of patients to receive either standard dose ("Noise index": 26 (SMARTmA); 120 KV ) or low dose ("Noise index": 26 (SMARTmA); 80 KV) or very low dose ("Noise index": 30 (SMARTmA); 80 KV). Sample size was based on the purpose of the study, represented by score obtained for the image quality.
In detail, patients assigned to the standard dose form the calibration group, in which the proportion of segments whose score was at least 2 was expected to be equal to 95%. The calibration group was not a control group in the traditional sense and a formal efficacy comparison between the investigational treatment groups and the calibration group was not planned. Results obtained in the calibration arm were used to judge the results obtained in the experimental arm as follows:

<table>
<thead>
<tr>
<th>Calibration arm</th>
<th>Experimental arms</th>
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<tbody>
<tr>
<td></td>
<td>Positive result</td>
</tr>
<tr>
<td><strong>Better than expected</strong></td>
<td>High risk of false result; second trial recommended</td>
</tr>
<tr>
<td><strong>As expected</strong></td>
<td>Positive result</td>
</tr>
<tr>
<td><strong>Worse than expected</strong></td>
<td>Positive result</td>
</tr>
</tbody>
</table>

Primary analysis was performed on an intention to treat basis, therefore segments of all the randomized patients satisfying eligibility criteria were analyzed. Major violations in the eligibility criteria and study conduct were evaluated on a case by case basis in a pre-analysis meeting in order to define the population to be analysed. Segments from patients withdrawn due to treatment related reasons were included in the analysis with a score <2.

The analysis was separately performed for each of the two experimental doses.

The proportion of segments with a score is ≥2 was stated at a minimum desirable of 75%, while it was not acceptable at a level <60%. Using the design proposed by A'Hern for the binomial distribution, setting the probability of erroneously concluding that the proportion of complete response was >70% at 10% (one-sided \( \alpha = 0.091 \)) and the probability of correctly concluding that this proportion was at least 85% at 90% (\( \# = 0.099 \)), it was necessary to evaluate 53 segments. Assuming a randomization ratio of 1:1:1 (standard dose : low dose : very low dose), a 10% drop-out rate, and expecting about 4 segments per patient it will be necessary to randomized approximately at least 45 patients (15 in each random arm).

The three X-ray exposure acquisition protocols were compared in terms of quantitative and qualitative as well as diagnostic performance results by using t-tests for paired data.

Interobserver agreement in the evaluation of CTA in terms of diagnostic performance was assessed using linear weighted kappa (k) statistics. The k values were interpreted as follows: 0.01-0.20, slight agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, good agreement; 0.81-.1.00, excellent agreement.

Statistical analyses were carried out using SAS release 9.2.
Results

Study Population

A total of 60 consecutive adult patients (46 male, 14 female; mean age: 70.8±11.5 years; range: 40-95 years) were prospectively enrolled. The mean height and weight of the patients were 168.5±7.5 cm (range: 160-184 cm) and 72.6±11 kg (range: 42-92 kg), respectively. The mean BMI was 25.4±3.1 kg/m$^2$ (range: 18.7-29.9 kg/m$^2$). No patients were in BMI category 1 or 4, while 35 were in category 2, 25 in category 3. No significant differences were found between the three groups in terms of epidemiologic characteristics (Table I on page ).

MDCTA Examinations

All MDCTA examinations were considered technically adequate with no interference due to the presence of artifacts. No adverse events were recorded.

Evaluation of Image Noise

In the aortic lumen, the mean attenuation obtained for the standard-dose protocol was 365.36±63.44 (circular ROIs of 10.55±0.43 cm$^2$) and the standard deviation of pixel values was 33.15±13.08. Conversely, for the low-dose and ultra-low-dose protocols the mean attenuation obtained were 575.64±174.28 (circular ROIs of 10.54 ± 0.48 cm$^2$) and 577.14±129.45 (circular ROIs of 10.55 ± 0.28 cm$^2$) and the standard deviation of pixel values were higher at 45.89±12.61 and 47.81±9.27, respectively (SD vs LD/ULD: p<.05).

In the gastric cavity, the standard deviation of pixel values was 33.05±34.71 (mean attenuation value: -926.64±50.21 HU, circular ROIs of 10.55±0.43 cm$^2$), 34.68±22.95 (mean attenuation value: -870.94±207.51 HU, circular ROIs of 10.54±0.48 cm$^2$), and 59.31±69.40 (mean attenuation value: -859.31±178.96 HU, circular ROIs of 10.53±0.28 cm$^2$), for the standard-dose, low-dose, and ultra-low-dose acquisition protocols, respectively (p>.05).

Regarding the subjective assessment of image graininess, a statistically significant difference was seen between the standard and low-dose/ultra-low-dose protocols on axial images (SDvsLD, SDvsULD: p<.001), whereas no significant differences were found on 3D reconstruction images (p>.05). No significant differences were found between low-dose and ultra-low-dose on both axial and 3D reconstruction images (p>.05).
(Table II on page ). However, in all cases significantly less noise was noted using the standard-dose protocol. A score of 5, indicating unacceptable noise, was never recorded.

**Evaluation of Image Quality**

None of the MDCTA image sets were considered of poor image quality. Although a mean arterial attenuation greater than 200 HU was obtained in all segments regardless of the acquisition protocol used, statistically significantly higher attenuation was determined for images obtained using the low-dose and ultra-low-dose acquisition protocols compared to the standard protocol (p<0.0001; all vascular segments). No significant differences were found between low-dose and ultra-low-dose (Table III on page ).

In the right psoas muscle, the standard-dose protocol resulted in a mean attenuation value of 51.92±8.81 HU (circular ROIs of 10.55±0.43 cm$^2$) and a standard deviation of pixel values of 24.63±8.16 while the corresponding values for the low-dose and ultra-low-dose protocols were 62.68±18.20 HU (circular ROIs of 10.54±0.48 cm$^2$) and 64.87±9.66 HU (circular ROIs of 10.55±0.28 cm$^2$) and 37.94±7.93 and 40.71±8.68, respectively.

Similar values were obtained for the left psoas muscle: the standard dose protocol resulted in a mean attenuation value of 53.71±10.39 (circular ROIs of 10.55±0.43 cm$^2$) and a standard deviation of pixel values of 23.78±8.01 while the low-dose and ultra-low-dose protocols resulted in a mean attenuation value of 66.93±11.98 (circular ROIs of 10.54±0.48 cm$^2$) and 69.23±12.55 (circular ROIs of 10.55±0.28 cm$^2$), and a standard deviation of pixel values of 36.16±4.66 and 38.71±9.96, respectively.

No statistically significant differences were found between the three protocols in terms of CNR (15.34±6.10 vs. 14.04±5.4 vs 14.37±4.33; p>.05).

The subjective assessment of image quality performed on axial images revealed statistically significantly higher values for the standard-dose protocol compared to the low-dose/ultra-low-dose protocol in all segments evaluated, with a mean qualitative contrast enhancement score of 3.44±0.71 compared to 3.21±0.53 and 3.19±0.72 (p<.05), whereas no significant differences were found when comparing standard-dose and low-dose or ultra-low-dose on 3D images as well as low-dose and ultra-low-dose protocols on both axial and 3D-images, respectively (Table IV on page ). (Fig.1 a-b on page , fig.1 c-g on page , fig.1 h-k on page , fig.1 l-m on page ; fig.2 a-b on page , fig.2 c-f on page ; fig.3 on page ; fig.4 on page ; fig.5 on page ; fig.6 on page ; fig.7 on page ; fig.8 on page ).

**Radiation Dose Estimation**
The total CTDIw was 12.96 mGy for the standard-dose protocol, 6.34 mGy for the low-dose protocol, and 5.89 mGy for the ultra-low-dose protocols, with an effective calculated dose of 29.32 mSv, 14.64 mSv, and 11.43 mSv, respectively. Thus, when compared to standard dose protocol, an overall dose reduction of 50% was observed for the low-dose protocol and 61% for the ultra-low-dose protocol, respectively.
Conclusion

In our study, we reduced both the tube current by using an automatic exposure control (Smart mA: Noise Index from 26 to 30) and the tube voltage (from 120 kV to 80 kV) and obtained an overall radiation dose reduction of 61%. Although decreases in both tube current and tube voltage are associated with a concomitant increase in image noise which may compromise image quality and negatively impact patient care, we succeeded in maintaining adequate image quality by combining the ultra-low-dose and low-dose protocols with the use of a contrast medium containing a high concentration of iodine (iomeprol 400). No differences were found on 3D reconstruction images between the three groups; in detail, no significant differences were found when comparing low-dose and ultra-low-dose protocols on both axial and 3D-images.

Concerning the contrast medium used for follow-up MDCTA in this study (iomeprol 400), the higher iodine concentration and correspondingly increased vascular attenuation was able to compensate for the increased image noise deriving from the reduced radiation dose to enable adequate depiction of the vascular anatomy. This increase in intravascular contrast largely offset the observed increase in image noise such that no statistically significant differences were apparent between the three protocols in terms of CNR.

In conclusion, this preliminary study demonstrates that an ultra-low-dose radiation exposure protocol is feasible for routine MDCT-angiography of peripheral artery for assessment of vascular occlusive disease. Increased image noise resulting from reduced radiation dose can be compensated for in terms of image quality and diagnostic performance through increasing the contrast attenuation with the use of contrast media containing higher concentrations of iodine.


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