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Image Quality and Radiation Exposure With a Low Tube Voltage Protocol for Coronary CT Angiography

Results of the PROTECTION II Trial

Jörg Hausleiter, MD,* Stefan Martinoff, MD,† Martin Hadamitzky, MD,* Eugenio Martuscelli, MD,‡ Iris Pschierer, MD,§ Gudrun M. Feuchtner, MD,‖ Paz Catalán-Sanz, MD,¶# Benedikt Czermak, MD,** Tanja S. Meyer, MD,* Franziska Hein, MD,* Bernhard Bischoff, MD,* Miriam Kuse,* Albert Schömig, MD,* Stephan Achenbach, MD††

Munich, Landshut, and Erlangen, Germany; Rome, Italy; Innsbruck, Austria; Oviedo and Barcelona, Spain

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OBJECTIVES The purpose of this study was to evaluate image quality and radiation dose using a 100 kVp tube voltage scan protocol compared with standard 120 kVp for coronary computed tomography angiography (CTA).

BACKGROUND Concerns have been raised about radiation exposure during coronary CTA. The use of a 100 kVp tube voltage scan protocol effectively lowers coronary CTA radiation dose compared with standard 120 kVp, but it is unknown whether image quality is maintained.

METHODS We enrolled 400 nonobese patients who underwent coronary CTA: 202 patients were randomly assigned to a 100 kVp protocol and 198 patients to a 120 kVp protocol. The primary end point was to demonstrate noninferiority in image quality with the 100 kVp protocol, which was assessed by a 4-point grading score (1 = nondiagnostic, 4 = excellent image quality). For the noninferiority analysis, a margin of −0.2 image quality score points for the difference between both scan protocols was pre-defined. Secondary end points included radiation dose and need for additional diagnostic tests during follow-up.

RESULTS The mean image quality scores in patients scanned with 100 kVp and 120 kVp were 3.30 ± 0.67 and 3.28 ± 0.68, respectively ($p = 0.742$); image quality of the 100 kVp protocol was not inferior, as demonstrated by the 97.5% confidence interval of the difference, which did not cross the pre-defined noninferiority margin of −0.2. The 100 kVp protocol was associated with a 31% relative reduction in radiation exposure (dose-length product: 868 ± 317 mGy × cm with 120 kVp vs. 599 ± 255 mGy × cm with 100 kVp; $p < 0.0001$). At 30-day follow-up, the need for additional diagnostic studies did not differ (13.4% vs. 19.2% for 100 kVp vs. 120 kVp, respectively; $p = 0.114$).

CONCLUSIONS A coronary CTA protocol using 100 kVp tube voltage maintained image quality, but reduced radiation exposure by 31% as compared with the standard 120 kVp protocol. Thus, 100 kVp scan protocols should be considered for nonobese patients to keep radiation exposure as low as reasonably achievable. (Prospective Randomized Trial on Radiation Dose Estimates of Cardiac CT Angiography in Patients Scanned With a 100 kVp Protocol [PROTECTION II]; NCT00611780) (J Am Coll Cardiol Img 2010;3:1113–23) © 2010 by the American College of Cardiology Foundation

Coronary computed tomography angiography (CTA) has emerged as a useful diagnostic imaging modality for the noninvasive assessment of coronary artery disease with accepted clinical indications in selected patient groups (1). With the constantly increasing number of coronary CTA-capable scanners worldwide, the volume of coronary CTA scans performed is likely to increase. Although the individual risk for radiation induced cancer is small relative to the gain of

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diagnostic information for most coronary CTA studies, coronary CTA will contribute to the overall burden of medical radiation exposure (2). Accordingly, new strategies to obtain diagnostic coronary CTA images with the lowest possible radiation exposure need to be developed and validated before they will become widely applied.

Coronary CTA is usually performed with an X-ray tube voltage of 120 kVp. Data acquisition at a reduced tube voltage of 100 kVp is possible and has been suggested as an effective means to lower radiation dose in nonobese patients without compromising diagnostic coronary CTA image quality (3). However, recent studies have demonstrated an infrequent use of this dose-reduction strategy in daily practice (4), which is most likely explained by 1) a lack of awareness regarding this strategy; 2) a lack of scientific data demonstrating maintained image quality and level of diagnostic confidence; and 3) lack of standardized recommendations concerning its use in clinical practice. Consequently, the primary objective of this randomized study was to demonstrate the noninferiority of a 100 kVp scan protocol for coronary CTA in terms of image quality when compared with the conventional 120 kVp scan protocol. The secondary objectives were to compare radiation doses for coronary CTA and clinical outcome with the use of a 100 kVp and 120 kVp scan protocol.

ABBREVIATIONS AND ACRONYMS

BMI = body mass index

CTA = computed tomography angiography

$CTDI_{vol}$ = volume computed tomography dose index

DLP = dose-length product

METHODS

Study protocol. The PROTECTION II (Prospective Randomized Trial on Radiation Dose Estimates of Cardiac CT Angiography in Patients Scanned With a 100 kVp Protocol) study is an international, multicenter, investigator-driven study that randomly allocated patients undergoing clinically indicated coronary CTA for suspected coronary artery disease at 8 study sites to either a 100 kVp or a 120 kVp tube voltage scan protocol. Patients with stable sinus rhythm and a body weight of <90 kg or body mass index of <30 kg/m^2 were eligible for this study. Exclusion criteria were patients with known coronary artery disease, extensive coronary artery calcifications with an Agatston score equivalent of >800 units (if calcium scoring has been performed), coronary CTA for noncoronary indication, and non–electrocardiography (ECG)-triggered or non–ECG-gated coronary CTA studies. The study protocol had been approved by the local ethics committee. Written informed consent was obtained from each patient before enrollment in the study.

Study design and coronary CTA. Patients were randomly assigned to a 100 kVp or a 120 kVp tube voltage scan protocol by means of sealed envelopes. Separate randomization blocks were used for the participating institutions to allow for a comparable number of patients for each computed tomography (CT) manufacturer. At 8 participating study sites, the following 64-slice CT systems were used: LightSpeed VCT (1 site) and LightSpeed VCT XT (1 site [GE Healthcare, Waukesha, Wisconsin]); Somatom Sensation 64 (1 site) and Somatom Definition (2 sites [both Siemens Medical Solutions, Forchheim, Germany]); and Aquilion 64 (3 sites [Toshiba Medical Systems, Otawara-shi, Tochigi, Japan]).

The administration of beta-blockers was recommended to obtain heart rates <60 beats/min and 70 beats/min in patients studied with single-source and dual-source CT systems, respectively. Coronary

From the *Klinik für Herz- und Kreislauferkrankungen, Deutsches Herzzentrum München, Klinik an der Technischen Universität München, Munich, Germany; †Institut für Radiologie und Nuklearmedizin, Deutsches Herzzentrum München, Klinik an der Technischen Universität München, Munich, Germany; ‡Department of Cardiology, Tor Vergata University, Rome, Italy; §Medizinische Klinik I, Krankenhaus Landshut-Achdorf, Landshut, Germany; ‖Universitätsklinik Radiologie II, Medizinische Universität Innsbruck, Innsbruck, Austria; ¶Centro Médico de Asturias, Oviedo, Spain; #Hospital de la Santa Creu i Sant Pau and Clínica Creu Blanca, Barcelona, Spain; **Universitätsklinik Radiologie I, Medizinische Universität Innsbruck, Innsbruck, Austria; and ††Medizinische Klinik 2, Universitätsklinikum Erlangen, Erlangen, Germany. This study was supported by an unrestricted financial research grant from Siemens Medical Solutions, Forchheim, Germany. All data and information in this manuscript were controlled by the authors. Drs. Hausleiter and Achenbach reported receiving research grants from Siemens Medical Systems unrelated to the current study. Dr. Achenbach was supported by a grant from the German "Bundesministerium für Bildung und Forschung" (BMBF 01 EV 0708). All other authors report that they have no relationships to disclose.

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vasodilation with the use of oral nitrates was also recommended. Before randomization, a localizer was acquired for planning of subsequent scan ranges and, if indicated, a nonenhanced scan for coronary artery calcium scoring was performed. Coronary CTA was carried out with scanner settings and with the contrast injection protocols at the discretion of the local study investigator. Randomization envelopes, which were opened before the coronary CTA, determined the tube voltage (100 kVp or 120 kVp). The study protocol recommended leaving all scan parameters including the level of the tube current unchanged. The use of other strategies for radiation dose reduction, including ECG-controlled modulation of the tube current in ECG-gated spiral data acquisition or an ECG-triggered sequential scan technique was recommended when appropriate.

After data acquisition, the local study investigators reconstructed the axial images as established at the study site and as needed for clinical decision making. Image reconstruction including the selection of the cardiac phase with the lowest motion, the applied reconstruction kernel, and technique were at the discretion of the investigator. The study protocol asked to send all available axial data sets that had been reconstructed for clinical decision making to the study core laboratory for analysis of image quality.

Study end points. The primary end point of the study was image quality, assessed with an image quality score. Secondary end points included radiation dose and quantitative image quality parameters. Furthermore, the need for subsequent cardiac tests including stress testing (stress echocardiography, stress nuclear cardiac perfusion imaging, or stress cardiac magnetic resonance) and invasive coronary angiography within 30 days after coronary CTA was assessed as clinical end point. The follow-up protocol after coronary CTA consisted of a telephone interview at 30 days.

Data analysis. All data sets were evaluated in the coronary CTA core laboratory by 2 experienced operators (F.H. and T.M.) who were unaware of the assigned scan protocol. The data sets were made anonymous and were randomly assessed to avoid any bias. The operator's expertise included 3 years (F.H.) and 5 years (T.M.) of coronary CTA interpretation with >500 coronary CTA studies per year. The data sets were assessed on axial slices, multiplanar reformations, and thin-slab maximum intensity projections.

Image quality of 4 main coronary arteries (left main, left anterior descending, left circumflex, and right coronary artery) was determined based on a 4-point grading system (Fig. 1) (5), as follows: score 1, nondiagnostic: impaired image quality that precluded appropriate evaluation of the coronary arteries due to severe motion artifacts, extensive coronary calcifications, severe image noise, or insufficient contrast; score 2, adequate: reduced image quality because of artifacts due to motion, image noise, or low contrast attenuation, but sufficient to rule out significant stenosis; score 3, good: presence of artifacts caused by motion, image noise, coronary calcifications, or low contrast, but fully preserved ability to assess the presence of luminal stenosis as well as the presence of calcified and noncalcified coronary atherosclerotic plaque; score 4, excellent: complete absence of motion artifacts, strong attenuation of vessel lumen, and clear delineation of vessel walls, with the ability to assess luminal stenosis as well as plaque characteristics.

Each coronary artery, including their side branches with a minimum diameter of at least 1.5 mm, was assigned a score from 1 to 4 by 2 experienced observers; and image quality was determined by averaging the scores of the 4 coronary arteries, avoiding intrapatient correlations. In case of disagreement between the 2 observers, final assessment was made by an experienced third reader. In addition, coronary CTA studies with an assigned score of 1 in any coronary artery were defined as nondiagnostic studies.

Signal intensity, image noise, signal-to-noise ratio, and contrast-to-noise ratio were quantified as objective image quality parameters. All measurements were performed (by F.H.) on reformatted axial images with a slice thickness of 1.0 mm to allow for comparable measurements between different CT systems. Signal intensity was derived from the mean CT attenuation values (Hounsfield units) averaged from 2 circular regions of interest (size >7 mm^2) in the proximal segments of the left and right coronary artery lumen. Image noise was defined as the averaged standard deviations of the CT attenuation values within these 2 regions of interest. The signal-to-noise ratio was calculated as mean CT attenuation values of the left and right coronary arteries divided by the image noise. The contrast-to-noise ratio was defined as the difference between the mean CT attenuation values of the proximal coronary arteries and the mean density of the left lateral ventricular wall, which was divided by image noise.

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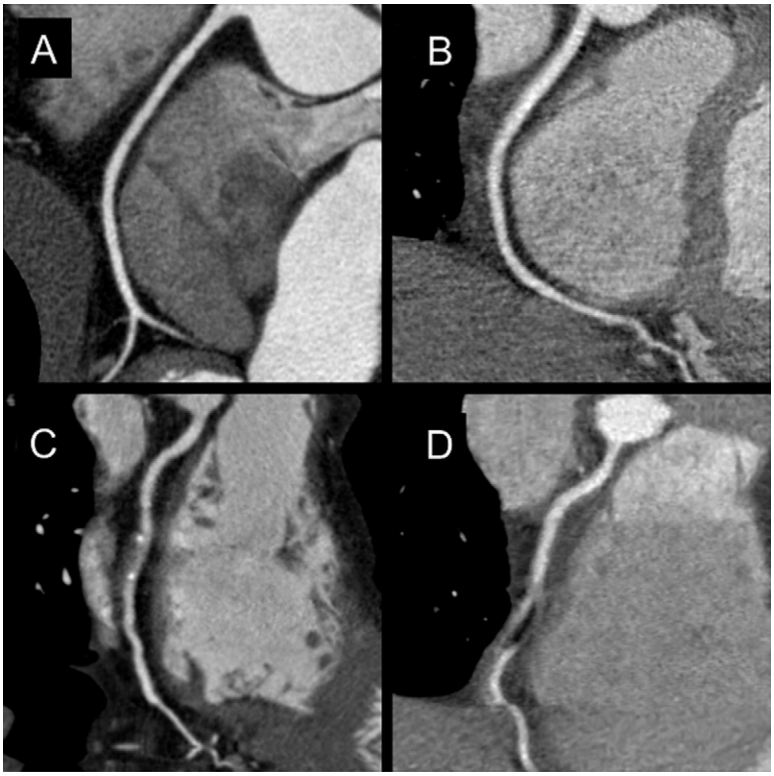

Figure 1. **Examples of Different Image Quality Scores**

Representative examples for the different image quality scores. The examples show curved multiplanar reformations of right coronary arteries of different patients: **(A)** displays "excellent" image quality, **(B)** "good" image quality, **(C)** "adequate" image quality, and **(D)** "non-diagnostic" image quality.

Estimation of radiation dose. The study investigators obtained the parameters relevant to radiation dose including volume CT dose index ($CTDI_{vol}$) and dose-length product (DLP) from the scan protocol generated by the CT system after each coronary CTA study. The effective dose of coronary CTA can be estimated by a method proposed by the European Working Group for Guidelines on Quality Criteria in CT (6). The effective dose is derived from the product of the DLP and an organ weighting factor for the chest as the investigated anatomic region. This organ weighting factor ($k = 0.014$ $mSv \cdot mGy^{-1} \cdot cm^{-1}$) is averaged between male and female models. This weighting factor is considered to be derived from the most self-consistent and reliable data set (7).

Statistical analysis. The objective of the study was to assess the noninferiority of a 100 kVp to a 120 kVp scan protocol. Sample size calculation was based on a margin of noninferiority for image quality score set at −0.20. In the absence of published data, this margin was selected because we consider a larger difference as clinically relevant. Based on core laboratory data of the PROTECTION I (Prospective Multicenter Study On Radiation Dose Estimates Of Cardiac CT Angiography In Daily Practice) study (5), the assumed common standard deviation (SD) was 0.65. With a power of 80% and a 1-sided α-level of 0.025, we estimated that 167 patients in both groups were needed to show the noninferiority of the 100 kVp scan protocol. To compensate for unforeseeable scanning problems, we aimed to enroll a total of 400 patients (200 in each treatment arm). Sample size calculation was performed with nQuery Advisor (Statistical Solutions, Cork, Ireland). The analysis of primary and secondary end points was planned to be performed on an intention-to-diagnose basis. Results are expressed as counts (or proportions in percent) or as means (± SD). Continuous and categorical variables were analyzed with a 2-sided *t* test and chi-square test as appropriate. Pearson correlation coefficient was determined to quantify the agreement of observer 1 and 2 for image quality ratings before adjudication by the third observer. Univariable and multiple-variable linear regression models with backward elimination were used to identify predictors for image quality. The "R Project for Statistical Computing" was used for statistical analysis (7). Statistical significance was defined as $p < 0.05$.

RESULTS

Patient and coronary CTA characteristics. A total of 400 patients were enrolled between January and October 2007 in 8 participating institutions: 202 patients were randomly assigned to a 100 kVp scan protocol, and 198 patients were randomly assigned to a 120 kVp scan protocol. Patient and coronary CTA characteristics are shown in Table 1. With a mean body weight of 72.9 ± 10.6 kg and a mean height of 1.70 ± 0.08 cm, the overall mean body mass index (BMI) was 25.3 ± 2.9 kg/m^2 (median BMI [interquartile range]: 22.9 kg/m^2 [22.9 to 22.9 kg/m2]). Both groups were well matched regarding the used 64-slice CT systems, heart rate, and scan length. The majority of scans were performed with a retrospectively ECG-gated spiral data acquisition, whereas prospectively ECG-triggered sequential scan protocols were used in 6.8% of patients. The ECG-gated spiral and ECG-triggered sequential scan protocols were evenly distributed in the 100 kVp and 120 kVp scan protocols. No significant differences were observed regarding patient characteristics or coronary CTA protocols between groups.

Coronary CTA image quality. The assessment of the image quality score correlated well between the 2 primary image readers (correlation coefficient: 0.869; $p < 0.0001$). The mean image quality score was 3.30 ± 0.67 in the cohort scanned with 100 kVp, and 3.28 ± 0.68 in the cohort scanned with 120 kVp ($p = 0.742$) (Fig. 2). As a consequence, diagnostic noninferiority of the 100 kVp protocol was demonstrated since the upper margin of the 1-sided 97.5% confidence interval did not cross the pre-defined noninferiority margin of −0.2 score points ($p < 0.001$) (Fig. 3). The mean image quality scores for each coronary artery are summarized in Table 2. Figure 4 shows representative examples of 2 coronary CTAs acquired at 100 kVp (Fig. 4A) and 120 kVp (Fig. 4B).

Motion artefacts and low contrast were the main reasons for a nondiagnostic image quality score (score = 1) in 97% and 3% of nondiagnostic coronary arteries, respectively. Extensive coronary calcifications and increased image noise were not identified as reasons for nondiagnostic image quality. Nondiagnostic coronary CTA studies (image quality score = 1 in any coronary artery) were observed in 15.3% and 16.2% of 100 kVp and 120 kVp scans, respectively ($p = 0.823$). In these patients, the mean heart rate was significantly higher than in patients with diagnostic coronary CTA image quality (64.7 ± 9.2 beats/min vs.

Table 1. Patient and Coronary CTA Characteristics

Characteristic	100 kVp (202 Patients)	120 kVp (198 Patients)	p Value
Age, yrs	58.9 ± 11.6	60.5 ± 10.8	0.163
Male sex	108 (53.5)	110 (55.6)	0.675
Height, m	1.70 ± 0.08	1.70 ± 0.09	0.868
Weight, kg	72.6 ± 10.4	73.3 ± 10.8	0.505
Body mass index, kg/m^2	25.2 ± 3.0	25.3 ± 2.8	0.569
Beta-blocker administration before coronary CTA			0.763
Without	42 (20.8)	47 (23.7)	
Oral	76 (37.6)	70 (35.4)	
IV	84 (41.6)	81 (40.9)	
Heart rate, beats/min	57.6 ± 8.1	58.1 ± 7.6	0.519
Scan length, mm	123.1 ± 13.8	123.2 ± 14.3	0.950
64-slice CT systems			0.886
GE Healthcare	61 (30.2)	61 (30.8)	
Siemens	67 (33.2)	69 (34.8)	
Toshiba	74 (36.6)	68 (34.4)	
Data acquisition			0.884
Retrospective ECG-gated spiral	188 (93.1)	185 (93.4)	
Prospective ECG-triggered sequential	14 (6.9)	13 (6.6)	
ECG-controlled tube current modulation in spiral data acquisition	127 (67.6)	131 (70.8)	0.496

Data are n (%) or mean ± SD.
CT = computed tomography; CTA = computed tomography angiography; ECG = electrocardiogram; IV = intravenous.

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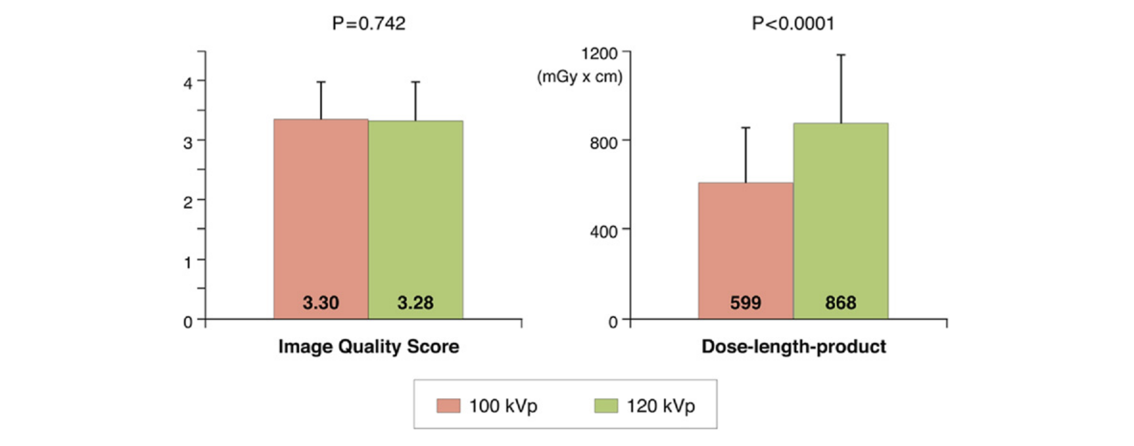

Figure 2. Image Quality Score and Estimated Radiation Dose

Image quality score and estimated radiation dose in the 100 kVp **(gray bars)** and 120 kVp **(black bars)** tube voltage coronary computed tomography angiography (CTA) scan groups.

56.7 ± 7.0 beats/min for patients with nondiagnostic vs. diagnostic coronary CTA image quality, respectively; $p < 0.0001$).

In pre-specified subgroup analyses, no significant differences in image quality score were observed between the different 64-slice CT systems for 100 kVp versus 120 kVp scans, respectively (GE: 3.30 ± 0.58 vs. 3.21 ± 0.64, p = 0.431; Siemens: 3.24 ± 0.77 vs. 3.25 ± 0.70, p = 0.953; and Toshiba: 3.36 ± 0.63 vs. 3.37 ± 0.69, p = 0.907). Furthermore, no significant differences in image quality score were observed between retrospectively ECG-gated spiral and prospectively ECG-triggered sequential data acquisitions for 100 kVp versus 120 kVp scans, respectively (ECG-gated spiral: 3.32 ± 0.67 vs. 3.28 ± 0.69, p = 0.628; and ECG-triggered sequential: 3.11 ± 0.61 vs. 3.24 ± 0.53, p = 0.543). Finally, no significant differences in image quality scores were observed between different BMI categories, stratified according to the third BMI quartile for 100 kVp versus 120 kVp scans, respectively (<27.1 kg/m^2: 3.35 ± 0.66 vs. 3.30 ± 0.66, p = 0.501; and ≥27.1 kg/m^2: 3.17 ± 0.68 vs. 3.23 ± 0.72, p = 0.657).

Radiation exposure. Table 2 shows the results for the radiation exposure with both scan protocols.

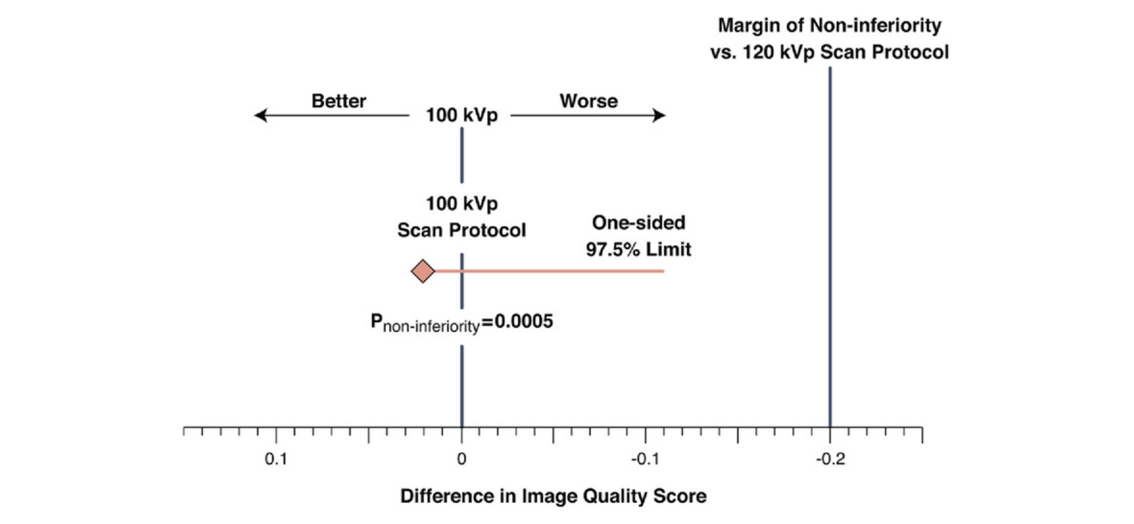

Figure 3. Noninferiority of 100 kVp Scan Protocol

Noninferiority of the 100 kVp scan protocol depicted as the difference in image quality score between the 100 kVp scan protocol and 120 kVp scan protocol.

The mean $CTDI_{vol}$ was significantly lower for the 100 kVp scan protocol (42.6 ± 19.5 mGy) than for the 120 kVp scan protocol (62.6 ± 26.1 mGy, $p < 0.0001$). Similarly, the mean DLP was significantly lower for the 100 kVp scan protocol (599 ± 255 mGy · cm for the 100 kVp protocol vs. 868 ± 317 mGy · cm for the 120 kVp protocol, $p < 0.0001$). This corresponds to a relative 31% reduction in estimated radiation dose for the 100 kVp tube voltage scan protocol ($p < 0.0001$) (Fig. 2). In the subgroup analysis, the 100 kVp scan protocol relatively reduced the DLP by 31% and 39% with retrospectively ECG-gated spiral and prospectively ECG-triggered sequential data acquisitions, respectively (DLP ECG-gated spiral: 629 ± 236 mGy · cm vs. 908 ± 288 mGy · cm, $p < 0.0001$; and DLP ECG-triggered sequential: 183 ± 78 mGy · cm vs. 299 ± 62 mGy · cm, $p = 0.0002$) for 100 kVp versus 120 kVp scans, respectively.

Clinical follow-up. Thirty-day clinical follow-up was completed in all patients. During follow-up, 27 patients of the 100 kVp group underwent additional testing for suspected obstructive coronary artery disease (20 patients with invasive coronary angiography, 4 patients with stress nuclear cardiac perfusion imaging, and 3 patients with stress cardiac magnetic resonance). In the 120 kVp group, 38 patients underwent subsequent additional tests (32 patients with invasive coronary angiography, 4 patients with stress nuclear cardiac perfusion imaging, and 2 patients with stress cardiac magnetic resonance). Consequently, the need for additional tests did not differ significantly between both groups (13.4% vs. 19.2% for 100 kVp vs. 120 kVp scan protocols, respectively; $p = 0.114$). No significant differences in image quality score were observed between patients with and without need for additional diagnostic testing (with additional diagnostic testing: 3.28 ± 0.54 vs. 3.32 ± 0.60, $p = 0.759$; and without additional diagnostic testing: 3.30 ± 0.68 vs. 3.27 ± 0.70, $p = 0.633$) for 100 kVp versus 120 kVp scans, respectively.

Quantitative image quality parameters. Quantitative image quality data that were analyzed as secondary end points are summarized in Table 3. Figure 5 illustrates representative measurements of 2 coronary CTAs acquired at 100 kVp (Fig. 5A) and 120 kVp (Fig. 5B). While signal intensity and image noise increased significantly with the 100 kVp scan protocol, a significant reduction of the signal-to-noise ratio was observed (11% relative reduction; $p = 0.003$). Similarly, the 100 kVp scan protocol displayed a trend toward a lower contrast-to-noise ratio (8% relative reduction; $p = 0.060$).

Predictors for image quality. The results of the univariate and multivariate linear regression analysis are summarized in Table 3. In the univariate anal-

Table 2. Results on Image Quality and Radiation Exposure

	100 kVp (202 Patients)	120 kVp (198 Patients)	p Value
Image quality score	3.30 ± 0.67	3.28 ± 0.68	0.742
Artery-based image quality score			
Left main coronary artery	3.77 ± 0.52	3.80 ± 0.46	0.480
Left anterior descending coronary artery	3.22 ± 0.82	3.23 ± 0.81	0.860
Left circumflex coronary artery	3.12 ± 0.86	3.10 ± 0.93	0.638
Right coronary artery	3.04 ± 1.02	2.99 ± 1.02	0.357
Signal intensity, HU	522 ± 109	432 ± 87	<0.0001
Image noise, HU	33.5 ± 12.5	24.6 ± 9.6	<0.0001
Signal-to-noise ratio	17.6 ± 7.1	19.8 ± 7.7	0.003
Contrast-to-noise ratio	13.6 ± 6.0	14.8 ± 6.4	0.060
$CTDI_{vol}$, mGy	42.6 ± 19.5	62.6 ± 26.1	<0.0001
Tube current for different CT systems			
General Electric, mA	768 ± 5	692 ± 109	<0.001
Siemens, mAs	484 ± 211	485 ± 213	0.987
Toshiba, mA	400 ± 53	338 ± 39	<0.001
DLP, mGy · cm	599 ± 255	868 ± 317	<0.0001
Effective dose estimate, mSv	8.4 ± 3.6	12.2 ± 4.4	<0.0001

Data are expressed as mean ± SD.
$CTDI_{vol}$ = volume computed tomography dose index; DLP = dose-length product; other abbreviation as in Table 1.

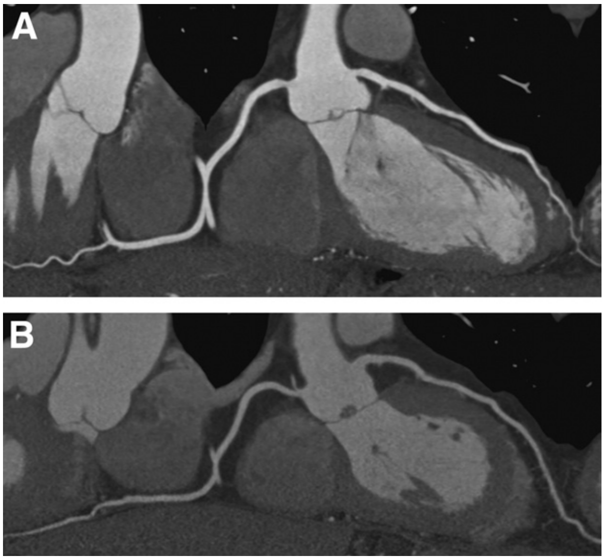

Figure 4. Curved Multiplanar Reformations

Representative images of curved multiplanar reformations of coronary computed tomography angiography scans acquired at 100 kVp **(A)** and 120 kVp **(B)**. Identical window level settings were applied.

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Table 3. Predictors for Image Quality Scores in the Univariate and Multivariate Linear Regression Analysis

	Univariate Analysis p Value	Multivariate Analysis p Value
Age	0.744	—
Male sex	0.184	—
Height	0.006	—
Weight	0.972	—
Body mass index	0.916	—
Beta-blocker administration before coronary CTA	0.005	—
Heart rate	<0.001	<0.001
Scan length	0.241	—
64-slice CT manufacturer	0.187	—
Data acquisition: retrospective spiral vs. prospective sequential	0.423	—
100 kVp tube voltage	0.660	—
Signal intensity	0.701	—
Image noise	0.021	—
Signal-to-noise ratio	0.516	—
Effective dose estimate	0.184	—

Abbreviations as in Table 1.

ysis, the height of the patient, administration of beta-blockers for coronary CTA, heart rate, and image noise were identified as predictors for image quality. In the multivariate analysis, applying a backward elimination model only heart rate was identified as strong predictor for image quality. Importantly, neither the tube voltage nor the estimated radiation exposure was identified as important factors predicting the image quality score.

DISCUSSION

In this prospective randomized study, we compared coronary CTA scan protocols employing either a 100 kVp or a 120 kVp tube voltage concerning image quality in normal weight to nonobese patients with suspected coronary artery disease. We could demonstrate that the use of a 100 kVp scan protocol for coronary CTA resulted in a similar and noninferior image quality when compared with the conventional 120 kVp scan protocol, while at the same time the estimated radiation dose was significantly lower.

Exposure to ionizing radiation has been criticized as a major limitation of coronary CTA (8). However, a recent worldwide radiation dose survey indicated that coronary CTA is associated with a median dose of 12 mSv (4), which needs to be compared with radiation doses of approximately 9 mSv and of as high as 41 mSv for sestamibi and thallium myocardial rest-stress nuclear scans, respectively (9). Accordingly, the mean radiation dose of 12.2 ± 4.4 mSv in the control group of the current study compares well with previous reports on estimated coronary CTA radiation dose. Within the last few years, a variety of strategies have been proposed to reduce the exposure to ionizing radiation during coronary CTA, including automated exposure control (10), ECG-controlled tube current modulation (3,11), and prospectively ECG-triggered sequential ("step-and-shoot") data acquisition (12–14). In pediatric CT, a reduced tube voltage has been shown to decrease ionizing radiation without affecting diagnostic image quality (15). Lowering tube voltage results in a considerable reduction in radiation dose, because under ideal conditions radiation dose varies in proportion to the square of the tube voltage (16). A reduced tube voltage of 100 kVp has also been proposed for coronary CTA in nonobese patients as an effective

Figure 5. Signal Intensity and Image Noise Measurements

Quantitative measurements of signal intensity (mean) and image noise (SD) in representative axial images of coronary computed tomography angiography scans acquired at 100 kVp **(A)** and 120 kVp **(B)**. Identical window level settings were applied.

means for radiation dose reduction (3); and several small nonrandomized studies have yielded encouraging results with a 100 kVp scan protocol for coronary CTA in terms of reduced radiation exposure and image quality (17,18). Similarly, the nonrandomized PROTECTION I dose survey indicated a preserved image quality with the 100 kVp scan protocol, while radiation exposure was considerably reduced (4). In this dose survey, the 100 kVp scan protocol was applied in only 5% of patients, which is likely explained by the facts that 1) the scan protocols recommended by CT manufacturers usually apply 120 kVp; and 2) it has not previously been clarified whether the level of diagnostic confidence and image quality are maintained with a 100 kVp scan protocol. Accordingly, the current randomized study compared a variety of end points germane to coronary CTA image quality when comparing 100 kVp and 120 kVp scan protocols. Designed as a noninferiority study, the image quality score, which was the primary study end point, did not differ significantly between both groups. Furthermore, the noninferiority analysis clearly demonstrated that the image quality of a 100 kVp scan protocol is not inferior to that of the conventional 120 kVp protocol, and thus, the level of diagnostic confidence is maintained with the 100 kVp scan protocol. Moreover, the finding of diagnostic equivalence of both scan protocols is supported by the nonsignificant difference in the clinical need for subsequent tests during follow-up.

In the current study, the mean exposure to ionizing radiation was significantly reduced from 12.2 mSv to 8.4 mSv with the 100 kVp scan protocol in nonobese patients, which translates into a 31% relative reduction in dose. These results are in keeping with previous nonrandomized studies (3). Furthermore, the results suggest that coronary CTA can be performed with a radiation exposure not dissimilar to that of invasive coronary angiography, which is likely to expose the patient to doses of approximately 7 mSv (9).

The 100 kVp scan protocol was associated with an increase in signal intensity and image noise. The increase in signal intensity is explained by the X-ray absorption characteristics of iodine, which are higher at lower kVp settings (19). With the concomitant increase in image noise, the resulting signal-to-noise and contrast-to-noise ratios were lower with the 100 kVp scan protocol. Image reconstruction was usually performed with the same reconstruction kernel for 100 kVp and 120 kVp images. It remains speculative whether dedicated 100 kVp image reconstruction kernels would improve image noise and consequently also signal-to-noise and contrast-to-noise ratios. Motion artifacts were the leading cause for nondiagnostic image quality, whereas increased image noise was not identified as reason for nonevaluability of the coronary arteries. Accordingly, our study demonstrates that while the observed changes in image noise and signal-to-noise ratio might influence the esthetic image quality, diagnostic image quality—as evaluated by the image quality scores—is not sacrificed. In fact, the current data support previous findings that a stringent control of the heart rate is of major importance for the level of diagnostic confidence and image quality in coronary CTA (20).

Study limitations. Numerous studies have shown the high diagnostic accuracy of 64-slice coronary CTA for the detection of significant coronary obstructions when compared with invasive coronary angiography. A recent meta-analysis of such studies, which applied primarily 120 kVp scan protocols, demonstrated sensitivity and specificity values of 97.5% and 91%, respectively, on a per-patient level (21). Although it would be desirable to demonstrate noninferiority of the 100 kVp scan protocol in terms of maintained sensitivity and specificity values, a sample size calculation yielded the need for enrolling >1,650 patients. Considering that the meta-analysis discussed in the preceding text included a total of only 875 patients who were enrolled in 13 studies comparing 64-slice coronary CTA and invasive angiography, the need for such a large patient population in a single study indicates the unfeasibility for such a noninferiority study protocol. Accordingly, we used the image quality score as alternative measure of noninferiority.

This study included patients with a low to intermediate risk for having obstructive coronary artery disease. Although the image quality was also comparable between 100 kVp and 120 kVp scans in the subgroup of patients with suspected coronary artery undergoing additional diagnostic testing during follow-up, it remains unproven if the current study results can be applied to patients being at high risk for having coronary artery disease or patients with advanced stages of coronary atherosclerosis.

The radiation dose associated with the localizer, the bolus timing scan, and with coronary calcium scoring, which is performed in some institutions before coronary CTA, was not assessed in the current study. However, compared with coronary CTA, the radiation dose of calcium scoring represents only a small fraction of the total dose of a cardiac CT study (22). Finally, the absence of calcium scores is recognized as limitation.

Implications. Based on the study findings, the use of a 100 kVp scan protocol is recommended for coronary CTA in nonobese patients with suspected coronary artery disease. It is important to realize that the 100 kVp scan protocol can be easily combined with other strategies for dose reduction, such as ECG-controlled tube current modulation, and prospectively ECG-triggered sequential data acquisition. The combination of such strategies will result in very efficacious dose reduction, when compared with standard spiral coronary CTA scan protocols.

Patient inclusion was limited to nonobese patients (body weight ≤90 kg or BMI ≤30 kg/m^2), because image noise increases with increasing body mass. Patients above these inclusion criteria might still qualify for a 100 kVp tube voltage protocol depending on the individual chest wall attenuation. As pointed out before, the 100 kVp tube voltage scan protocol was applied in only 5% of the 2007 dose survey population in the PROTECTION I study (4). The impact of the current study findings are evident when realizing that 78.9% or 81.8% of the PROTECTION I patients would have qualified for a 100 kVp coronary CTA scan protocol if a threshold ≤90 kg for body weight or ≤30 kg/m^2 for body mass index had been applied.

CONCLUSIONS

In conclusion, the PROTECTION II study demonstrates that image quality is maintained with the use of a 100 kVp tube voltage scan protocol for coronary CTA in nonobese patients with suspected coronary artery disease, while achieving a 31% relative reduction in estimated radiation dose. Consequently, the 100 kVp scan protocol should be considered for coronary CTA in all nonobese patients, in pursuit of the ultimate goal to obtain diagnostic coronary CTA images with the lowest possible radiation dose.

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Reprint requests and correspondence: Dr. Jörg Hausleiter, Deutsches Herzzentrum München, Lazarettstrasse 36, München 80636, Germany. *E-mail: hausleiter@dhm.mhn.de.*

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