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ORIGINAL RESEARCH

Application of Low Tube Potentials in CCTA

Results From the PROTECTION VI Study

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ABSTRACT

OBJECTIVES The aim of this study was to assess the use of low tube potentials for coronary computed tomography angiography (CCTA) in worldwide clinical practice and its influence on radiation exposure, contrast agent volume, and image quality.

BACKGROUND CCTA is frequently used in clinical practice. Lowering of tube potential is a potent method to reduce radiation exposure and to economize contrast agent volume.

METHODS CCTAs of 4,006 patients from 61 international study sites were analyzed regarding very-low (≤80 kVp), low (90 to 100 kVp), conventional (110 to 120 kVp), and high (≥130 kVp) tube potentials. The impact on dose-length product (DLP) and contrast agent volume was analyzed. Image quality was determined by evaluation of the diagnostic applicability and assessment of the objective image parameters signal-to-noise-ratio (SNR) and contrast-to-noise-ratio (CNR).

RESULTS When compared with conventional tube potentials, low tube potentials were used in 56% of CCTAs (≤80 kVp: 9%; 90 to 100 kVp: 47%), which varied among sites from 0% to 100%. Tube potential reduction was associated with low-cardiovascular risk profile, low body mass index (BMI), and new-generation scanners. Median radiation exposure was lowered by 68% or 50% and median contrast agent volume by 25% or 13% for tube potential protocols of ≤80 kVp or 90 to 100 kVp when compared with conventional tube potentials, respectively (all $p < 0.001$). With the use of lower tube potentials, the frequency of diagnostic scans was maintained ($p = 0.41$), whereas SNR and CNR significantly improved (both $p < 0.001$). Considering BMI eligibility criteria, 58% ($n = 946$) of conventionally scanned patients would have been suitable for low tube potential protocols, and 44% ($n = 831$) of patients scanned with 90 to 100 kVp would have been eligible for very-low tube potential CCTA imaging of ≤80 kVp.

CONCLUSIONS This large international registry confirms the feasibility of tube potential reduction in clinical practice leading to lower radiation exposure and lower contrast volumes. The current registry also demonstrates that this strategy is still underused in daily practice. (PROspective multicenter registry on radiaTion dose Estimates of cardiac CT angIOgraphy iN daily practice in 2017 [PROTECTION-VI]; NCT02996903) (J Am Coll Cardiol Img 2020;13:425–34)

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

CCTA = coronary computed tomography angiography

CNR = contrast-to-noise ratio

CT = computed tomography

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

DLP = dose-length product

SNR = signal-to-noise ratio

Coronary computed tomography angiography (CCTA) has emerged as a favorable diagnostic tool with high accuracy in the detection and exclusion of obstructive coronary artery disease (1–3). Furthermore, its use has been associated with a significant reduction in mortality and nonfatal myocardial infarction (4). The downside of CCTA imaging is the adverse exposure to potentially harmful ionizing radiation (5). The safety of CCTA has improved considerably during the last decade and median radiation exposure decreased by 78% as recently described in the PROTECTION VI (PROspective multicenter registry on radiaTion dose Estimates of cardiac CT angIOgraphy iN daily practice in 2017) study (6). Reduction in tube potentials from the conventional 120 kVp is a major contributor to this dose reduction.

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Several studies demonstrated the feasibility of a reduced potential to 100 kVp with maintenance of image quality (7–10). Additional experimental studies with a limited number of patients suggested very-low tube potentials down to 80 kVp or less with maintenance of diagnostic value and quantitative image quality parameters (11–14). The body mass index (BMI) has been acknowledged as an eligibility criterion for the application of reduced tube potentials in CCTA. In this regard, patients with a BMI <30 kg/m^2 should be selected for tube potential reduction from conventional 120 kVp to 100 kVp (10,15). The possibility of tube potential reduction in obese patients with a BMI >30 kg/m^2 has also been described, but only in small patient populations (16). An escalation of low tube potential imaging toward 80 kVp or less was proposed in several studies for patients with a BMI <25 kg/m^2 (12–14,17,18). However, the frequency in application and the magnitude of tube potential reduction in worldwide clinical practice are currently unknown. This predefined sub-analysis of the international, prospective, multicenter PROTECTION VI study has been designed to analyze the application of tube potential reduction protocols and their impact on radiation dose, contrast agent volume, and image quality in CCTA imaging.

METHODS

STUDY PROTOCOL. The methods of the PROTECTION VI study were described previously (19). In brief, 61 international study sites provided image data and scan protocols of consecutive CCTAs performed during 1 month in 2017. Image data and CCTA study details were collected and analyzed in a central CCTA core laboratory. The selection of the CCTA scan protocol including the tube potential and the volume of iodinated contrast medium was at the discretion of the performing physician and was carried out according to local standard of clinical care. Each study site consulted the local ethics committee to evaluate the study protocol prior to patient enrolment. All patients gave written informed consent as required at the individual sites. An Executive Steering Committee composed of a group of physicians with expertise in CCTA, clinical research, and statistics supervised the study. The study is registered at clinicaltrials.gov (NCT02996903).

IMAGE QUALITY. For standardization of quantitative image quality analysis, the axial datasets were reformatted in 1.0-mm slice thickness. Signal intensity, image noise, contrast, signal-to-noise ratio (SNR), and contrast-to-noise ratio (CNR) were determined in a central core laboratory as described (20). Local investigators graded the diagnostic image quality using a simplified image quality score. Each coronary artery (left main, left anterior descending, left circumflex, and right coronary artery) was determined to be of either diagnostic or nondiagnostic image quality. Nondiagnostic quality was defined by severe vessel blurring or vessel discontinuity secondary to reconstruction artifacts, which did not allow the exclusion of obstructive coronary lesions. CCTAs were considered as nondiagnostic when at least 1 coronary artery was of nondiagnostic image quality.

Clinical Medicine, Faculty of Health, Aarhus University, Aarhus, Denmark; and the [P]Minneapolis Heart Institute, Minneapolis, Minnesota. Dr. Leipsic is a consultant to and holds stock options in Circle CVI and HeartFlow; and has received fellow support from GE Healthcare outside the submitted work. Dr. Chen has received non-financial support from Canon Medical systems outside the submitted work. Dr. Bax has received grants from Biotronik, Medtronic, Boston Scientific, GE Healthcare, and Edwards Lifesciences outside the submitted work; and has received speaker fees from Abbott Vascular. Dr. Schmermund has received grants from Siemens outside the submitted work. Dr. Grove has received speaker honoraria or consultancy fees from Abbott, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, and Roche outside the submitted work. Dr. Hausleiter has received speaker honoraria and research support from Abbott Vascular and Edwards Lifesciences outside the submitted work. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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ESTIMATION OF RADIATION DOSE. The collected parameters relevant to radiation dose included the volume computed tomography (CT) dose index ($CTDI_{vol}$) and dose-length product (DLP), which were both obtained from the CT scan protocol. The DLP was the primary study outcome parameter. The calculation of the effective dose is based on the product of the DLP and an organ weighting factor for the chest $k = 0.014$ mSv/mGy × cm (21) or alternatively a proposed conversion factor for CCTA imaging $k = 0.026$ mSv/mGy × cm (22).

STATISTICAL ANALYSIS. Variables are expressed as counts with proportions or medians with interquartile ranges. Comparison of groups was performed with the Wilcoxon-Mann-Whitney *U* test or chi-square test as appropriate. Multiple comparisons of nonparametric variables were conducted with the Kruskal-Wallis chi-squared test, subsequent post hoc analysis was performed with the Dunn test, and p values were adjusted with the Holm method. A p value <0.05 was considered to be statistically significant. Statistical analysis was performed using R version 3.4.1.

RESULTS

CCTA TUBE POTENTIAL SELECTION IN CURRENT CLINICAL ROUTINE. In the PROTECTION VI study, a total of 4,006 patients from 61 different study sites underwent CCTA. Among these, 377 patients (9%) were scanned with a very-low tube potential protocol of ≤80 kVp, and 1,889 patients (47%) were scanned with a reduced tube potential of 90 to 100 kVp (**Central Illustration**). Conventional tube potential of 110 to 120 kVp was selected for 1,662 patients (42%) and tube potential was increased (≥130 kVp) in 78 cases (2%). The selection of reduced tube potential protocols varied significantly between study sites (**Central Illustration**). Accordingly, the selection of reduced tube potential ≤100 kVp ranged from 0% to 100% of CCTAs in study sites. On the one end, 5 study sites (8% of all sites) scanned the majority of patients (> 50%) with a very-low tube potential of ≤80 kVp. On the other end, 28 study sites (47% of sites) exclusively scanned >80 kVp.

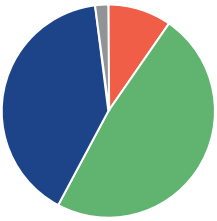
The application of tube potential reduction varied between vendors (**Figure 1**). Low tube potential protocols of 90 to 100 kVp were less frequently used with GE scanners (42% of CCTAs), when compared with all other vendors (Toshiba: 45%, Philips: 49%, Siemens: 50%; $p < 0.05$). The rate of very-low tube potential imaging of ≤80 kVp was significantly higher in Siemens scanners (17% of CCTAs) when compared with all other vendors (GE: 1%, Philips: 3%, Toshiba: 4%; $p < 0.001$). Regional differences in the application of low tube potential protocols are listed in Supplemental Table 1.

Patient and scan characteristics for all 4 groups of tube potential protocols (≤80 kVp, 90 to 100 kVp, 110 to 120 kVp, and ≥130 kVp) are summarized in **Table 1**. Although patient age did not vary between groups, very-low kVp was favored in female patients and patients with lower BMI. A reduced cardiovascular risk was significantly associated with the selection of lower tube potential, as observed by reduced frequency of hypertension, diabetes, dyslipidemia, and smoking history in CCTAs performed with ≤80 kVp protocols. Site experience expressed as the median duration of CCTA scanning in years varied between 11 and 12 years. The proportion of modern CT scanners (≥128 slices) was significantly increased with low tube potential scanning. Iterative image reconstruction as an additional dose-reduction strategy was more frequently used with very-low tube potential scanning (98% vs. 82% for ≤80 kVp vs. 110 to 120 kVp; $p < 0.001$), whereas the proportion of prospective scan techniques was similar (86% vs. 88% for ≤80 kVp vs. 110 to 120 kVp; $p = 0.39$).

REDUCTION OF RADIATION DOSE AND CONTRAST AGENT IN LOW TUBE POTENTIAL CCTA. When using conventional tube potential (110 to 120 kVp), the median $CTDI_{vol}$ added up to 22.8 (interquartile range [IQR]: 13.2 to 34.4) mGy. Application of low tube potential protocols significantly lowered the median $CTDI_{vol}$ to 11.1 (IQR: 6.3 to 16.6) mGy or 6.9 (IQR: 2.8 to 10.6) mGy using 90 to 100 kVp or ≤80 kVp protocols, respectively ($p < 0.001$). The median DLP for conventional 110 to 120 kVp scanning resulted in 310 (IQR: 182 to 468) mGy × cm and was reduced by 50% (156 [IQR: 88 to 236] mGy x cm) or even 68% (98 [IQR: 46 to 160] mGy × cm) with the use of 90 to 100 kVp or ≤80 kVp tube potential protocols (both $p < 0.001$) (**Figure 2A**). Consequently, median radiation dose for conventional tube potential imaging was estimated to be 4.3 (8.1) mSv when using the dose conversion factor $k = 0.014$ (or alternatively $k = 0.026$). The estimated median radiation dose was lowered to 2.2 (4.1) mSv or even 1.4 (2.5) mSv with the application of 90 to 100 kVp or ≤80 kVp tube potential protocols (both $p < 0.001$). In addition to the reduction of radiation dose, significantly less contrast agent volume was used with tube potential reduction. For CCTAs with a conventional tube potential of 110 to 120 kVp, median contrast agent volume added up to 80 (IQR: 70 to 100) ml and could be reduced by 13% (70 [IQR: 60 to 80] ml) or even 25% (60 [IQR: 55 to 79] ml) using 90 to 100 kVp or ≤ 80kVp protocols, respectively ($p < 0.001$) (**Figure 2B**).

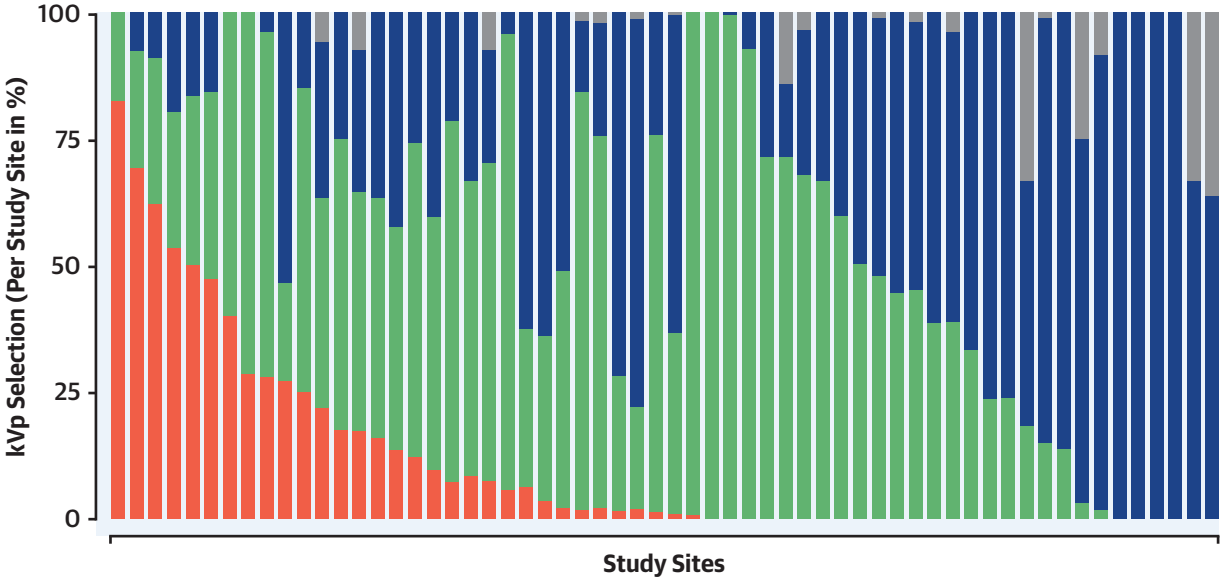
CENTRAL ILLUSTRATION **Application of Tube Potential Protocols in Current Clinical Routine CCTA Imaging**

A



Tube Potential	% (n)	DLP, mGy × cm	Contrast Agent, ml
≤80 kVp	9 (377)	98 (46-160)	60 (55-79)
90 - 100 kVp	47 (1,889)	156 (88-236)	70 (60-80)
110 - 120 kVp	42 (1,662)	310 (182-468)	80 (70-100)
≥130 kVp	2 (78)	632 (340-1,090)	90 (80-130)

B



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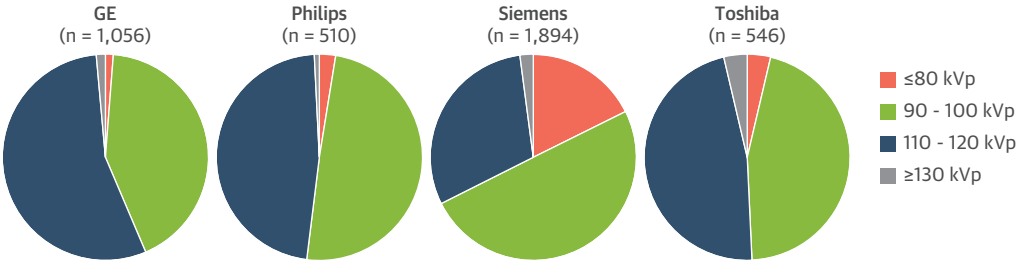
(A) Frequency of different tube potential protocols aggregated to ≤80 kVp, 90 to 100-kVp, 110 to 120 kVp, and ≥130 kVp. **(B)** Variation of tube potential protocol selection per study site. CCTA = coronary computed tomography angiography.

MAINTENANCE OF IMAGE QUALITY IN LOW TUBE POTENTIAL CCTA. Quantitative image quality parameters including median image noise, SNR, and CNR in reference to the selected tube potential are displayed in Table 2. Reduction of tube potential to 90 to 100 kVp or ≤80 kVp increased image noise by 6% or 23%, when compared with conventional 110 to 120 kVp CCTAs (both $p < 0.001$). However, the median SNR improved with tube potential reduction by 20% or 31% for 90 to 100 kVp or ≤80 kVp compared with 110 to 120 kVp scanning (both $p < 0.001$). Similarly, CNR improved by 25% or 39% with the use of 90 to 100 kVp or ≤80 kVp protocols (both $p < 0.001$). Importantly, the frequency of diagnostic scans was similar between all groups (97.6%, 98.4%, 97.8%, and 97.4% for ≤80 kVp, 90 to 100 kVp, 110 to 120 kVp, and ≥130 kVp, respectively; $p = 0.41$).

CAPACITY FOR TUBE POTENTIAL REDUCTION IN CLINICAL PRACTICE USING BMI ELIGIBILITY CRITERIA. To assess the capacity for further tube potential reduction in clinical practice, we analyzed the application of the different tube potential protocols by BMI eligibility criteria (Figure 3A). The majority of patients had a BMI <30 kg/m^2 (n = 2,940) and was eligible for the application of tube potential

FIGURE 1 Tube Potential Protocol Selection by CT Vendor



1% (n = 13)	3% (n = 13)	17% (n = 331)	4% (n = 20)	**≤80 kVp**
42% (n = 447)	49% (n = 252)	50% (n = 941)	45% (n = 249)	**90 - 100 kVp**
55% (n = 581)	47% (n = 241)	31% (n = 583)	47% (n = 257)	**110 - 120 kVp**
1% (n = 15)	1% (n = 4)	2% (n = 39)	4% (n = 20)	**≥130 kVp**

GE = General Electric Healthcare, Waukesha, Wisconsin; Philips = Philips Healthcare, Amsterdam, the Netherlands; Siemens = Siemens Medical Solutions, Forchheim, Germany; Toshiba = Toshiba Medical Systems Corporation, Ōtawara, Tochigi, Japan.

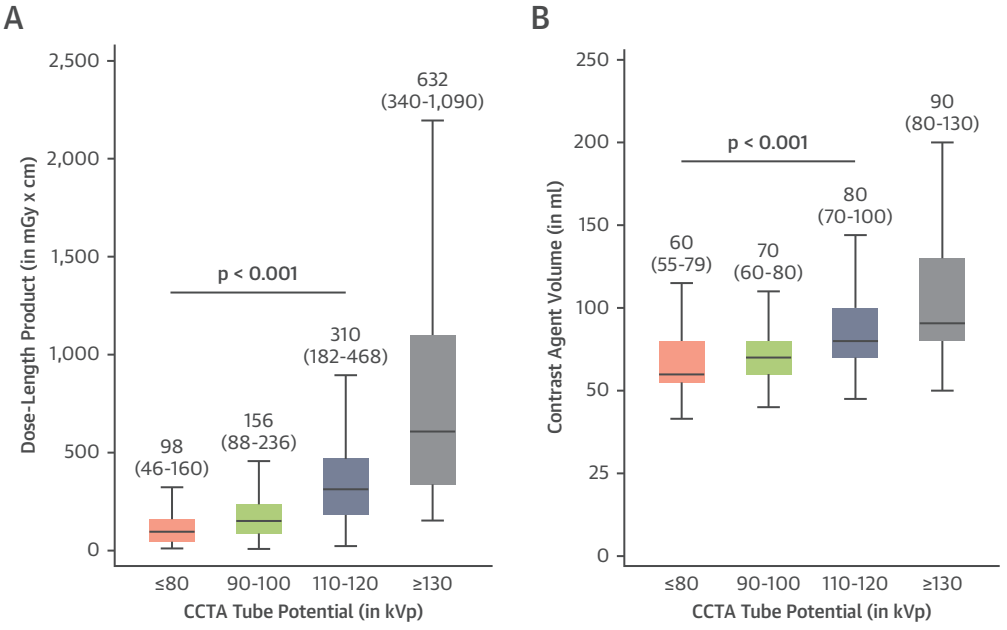
reduction. In fact, 67% of these patients were scanned with low tube potential protocols (90 to 100 kVp: 55%; ≤80 kVp: 12%). Patients with a BMI ≥30 kg/m^2 (n = 1,030) were mostly scanned with conventional tube potentials between 110 and 120 kVp (68% of patients), however, 26% of these patients were also scanned with low tube potentials (90 to 100 kVp: 24%; ≤80 kVp: 2%). A considerable subpopulation of patients had a BMI <25 kg/m^2 (n = 1,363). Only 19% of these patients (n = 256) were selected for eligible very-low tube potential protocols of ≤80 kVp. In an additional analysis, we calculated the BMI distribution by tube potential protocol (Figure 3B). In the conventional group without tube potential reduction (110 to 120 kVp), we identified 58% of patients (n = 946) with a BMI <30 kg/m^2 that would have been

TABLE 1 Patient and CCTA Scanning Characteristics

	≤80 kVp (n = 377)	90-100 kVp (n = 1,889)	110-120 kVp (n = 1,662)	≥130 kVp (n = 78)	p Value
Patient characteristics					
Age, yrs	61 (50-70)	59 (50-68)	59 (51-68)	59 (52-68)	0.71
Male, %	45 (166)	54 (1,027)	63 (1,048)	70 (55)	<0.001
Height, cm	167 (160-173)	168 (160-175)	171 (163-178)	175 (168-181)	<0.001
Weight, kg	65 (59-74)	73 (64-83)	85 (75-98)	108 (91-124)	<0.001
BMI, kg/m^2	24 (22-26)	26 (23-28)	29 (26-32)	35 (31-40)	<0.001
Hypertension, %	39 (149)	54 (1,026)	50 (825)	67 (52)	<0.001
Diabetes, %	10 (37)	14 (262)	18 (296)	22 (17)	<0.001
Dyslipidemia, %	36 (135)	32 (603)	46 (757)	47 (37)	<0.001
Smoker, %	11 (42)	18 (339)	16 (265)	19 (15)	0.0084
CCTA scanning characteristics					
Site experience, yrs	11 (10-13)	11 (8-13)	12 (8-14)	12 (8-14)	0.049
Modern CT (≥128 slices), %	99 (373)	94 (1783)	88 (1460)	73 (57)	<0.001
Scan length, mm	130 (119-140)	137 (124-144)	138 (130-142)	137 (124-142)	<0.001
Iterative reconstruction, %	98 (368)	81 (1,526)	82 (1,359)	68 (53)	<0.001
Scan technique, %					<0.001
Prospective	86 (322)	91 (1717)	88 (1457)	60 (47)	
Retrospective	14 (53)	9 (167)	12 (196)	40 (31)	

Values are median (interquartile range) or % (n).
BMI = body mass index; CCTA = coronary computed tomography angiography; CT = computed tomography.

FIGURE 2 Impact of Tube Potential Reduction on Dose-Length Product and Contrast Agent Volume in CCTA Imaging



Median dose-length product **(A)** and median contrast agent volume **(B)** per tube potential protocol. The middle horizontal line represents the median, the box shows the IQR, and error bars show the range of non-outlying data points **(whiskers)**. The **lower whisker** shows the lowest data point within the 25th percentile minus 1.5 times IQR and the **upper whisker** shows the highest data point within the 75th percentile plus 1.5 times IQR. IQR = interquartile range; other abbreviations as in Figure 1.

eligible for tube potential reduction to at least 100 kVp. In the group of CCTAs performed with 90 to 100 kVp, we identified 44% of patients (n = 831) with a BMI <25 kg/m^2 that would have qualified for additional escalation of tube potential ≤80 kVp.

DISCUSSION

CCTA has evolved to an important noninvasive tool for the evaluation of coronary artery disease in clinical routine. However, safety concerns remain in terms of exposure to ionizing radiation and the need for iodinated contrast agent with potential kidney damage. Consequently, several techniques to reduce radiation exposure and contrast agent volume have been developed during the last decade. The recently finalized international PROTECTION VI study revealed a median DLP of 195 mGy × cm for CCTA in current clinical practice with a considerable variation in dose between study sites (6). The PROTECTION VI study evaluated predictors for the magnitude of CCTA radiation exposure and identified body weight, heart

TABLE 2 CCTA Image Quality by Tube Potential Protocol

	≤80 kVp	90-100 kVp	110-120 kVp	≥130 kVp	p Value
Quantitative image quality					
Image noise, HU	39.6 (31.3-52.6)	34.3 (27.5-43.3)	32.3 (25.1-40.5)	28.0 (20.7-36.5)	<0.001
Signal intensity, HU	687 (566-796)	540 (450-624)	414 (356-473)	320 (294-357)	<0.001
CNR	13.3 (10.2-17.5)	12.0 (9.2-15.6)	9.6 (7.4-12.8)	8.5 (5.9-10.6)	<0.001
SNR	16.8 (12.9-21.8)	15.3 (12.0-19.4)	12.8 (10.0-16.6)	11.4 (8.4-15.2)	<0.001
Qualitative image quality					
Diagnostic scans, %	97.6 (360)	98.4 (1,840)	97.8 (1,524)	97.4 (76)	0.41

Values are median (interquartile range) or % (n).
CNR = contrast-to-noise ratio; HU = Hounsfield units; SNR = signal-to-noise ratio. Other abbreviation as in Table 1.

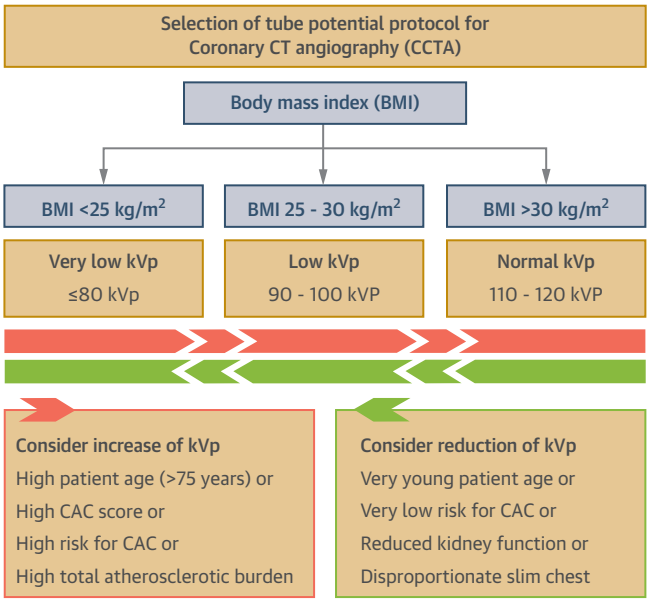
FIGURE 3 **Capacity for Low Tube Potential CCTA Imaging by BMI Eligibility Criteria**

(A) The application of respective tube potential protocols is demonstrated for different categories of BMI <30 kg/m² **(left)**, ≥ 30 kg/m² **(middle)**, or < 25 kg/m² **(right)**. **(B)** BMI distribution of scanned patients ranging from 10 to 50 kg/m² for the respective tube potential protocols of ≤80 kVp **(left)**, 90 to 100 kVp **(middle)**, and 110 to 120 kVp **(right)**. BMI = body mass index.

rate and rhythm, iterative image reconstruction, high-pitch helical scan technique, and tube potential reduction as independent predictors (6). The reduction of tube potential is extremely effective due to the exponential reduction of radiation dose. Additionally, iodine absorption is increased at lower tube potential settings, giving rise to advantages in iodinated contrast-enhanced CCTA imaging (23).

The current analysis of the PROTECTION VI study assessed the use of tube potential reduction in worldwide clinical practice and analyzed the impact of different tube potential reduction protocols on radiation dose, contrast agent volume, and image quality. Specifically, this study is the first report analyzing the worldwide feasibility and efficacy of very-low tube potential protocols down to 80 kVp and less in clinical routine imaging. The use of very-low tube potentials of ≤80 kVp was associated with a reduction of the mean DLP by 68% compared with conventional scanning with 120 kVp tube potential protocols. Low tube potential protocols between 90 and 100 kVp still lowered the mean DLP by 50%. Likewise, tube potential reduction lowered median contrast agent volume by 25% or 13% with the application of ≤80 kVp or 90 to 100 kVp protocols. The reduction of iodinated contrast agent during CCTA helps to protect kidney function on the one hand. On the other hand, iodinated contrast has been

FIGURE 4 Clinical Practice Guideline for the Selection of Tube Potential Protocols in CCTA Imaging



BMI eligibility criteria categorize the tube potential protocol. Additional factors may increase **(pink box)** or reduce **(green box)** the ideal tube potential category. CAC = coronary artery calcification; other abbreviations as in Figures 1 and 3.

demonstrated to amplify radiation-induced DNA damage, and thus the reduced contrast volumes add to the protection from radiation exposure (24).

Importantly, the feasibility of tube potential reduction regarding image quality was demonstrated in this study. As described in previous studies, low tube potential CCTA imaging leads to an increase of image noise because of the reduced penetration of photons at lower energy (14). This increase in image noise is a potential disadvantage because of a decrease of the overall image quality. However, tube potential reduction was associated with significant improvement of SNR and CNR due to the concomitant increase in signal and contrast, despite the reduced volume of contrast agent applied in low tube potential imaging. Hence, the reduction of tube potential may add to improved delineation of coronary lumen stenosis. Additionally, the rate of nondiagnostic CCTAs was unaffected by the selection of low tube potential protocols. However, low tube potential imaging with increased image noise might enhance blooming of coronary calcifications. Therefore, diagnostic accuracy of severely calcified coronary arteries with low tube potential imaging, particularly in combination with iterative image reconstruction, remains to be investigated.

This large registry revealed that a reduction of tube potential to 100 kVp or less was applied in 56% of CCTAs in current clinical routine. The majority of these patients were scanned with moderately reduced tube potential protocols between 90 and 100 kVp. In a way this can be interpreted as a success of the promotion of tube potential reduction strategies during recent years (7-10). However, we observed great variability in the application of low tube potential protocols ranging from 0% to 100%. Several sites followed a "one protocol fits all" strategy and excluded any variation in tube potential. In this regard, 4 participating sites in this study exclusively scanned using 120 kVp tube potential imaging. Very-low tube potential protocols of ≤80 kVp were applied in only 9% of CCTAs in clinical practice and are thus underrepresented in current clinical routine. Several contributing factors have been determined for the preference of very-low tube potential protocols of ≤80 kVp. First, the selection of very-low tube potential protocols was significantly influenced by the vendor of the installed CT system. The results of this study were obtained by the use of multiple vendors with a variety of commercially available CT scanners and are thus representative for real-world clinical routine imaging. Nevertheless, some hospitals might not have access to modern CT systems that are a prerequisite for very-low tube potential imaging. These technical circumstances might have also affected the results of this study. Second, the education and conventions at the individual study sites seem to contribute to the magnitude of tube voltage reduction. Regional differences in the selection of tube potential protocols have been identified. Many study sites rarely consider the application of very-low tube potential protocols, whereas, on the other hand, several study sites demonstrated that the majority of patients could be scanned with protocols of 80 kVp and less in clinical practice. Finally, the study demonstrated that clinicians select individual patients for very-low tube potential imaging. Practitioners seem to prefer both women and healthier patients as expressed by lower cardiovascular risk profiles for very-low tube potential imaging. Additionally, low BMI was significantly associated with the reduction of tube voltage. However, analysis of the BMI distribution revealed that a significant portion of patients would have been eligible for application and escalation of low tube voltage protocols. In this perspective, only 19% of patients that would have been eligible for very-low tube potential protocols (BMI <25 kg/m²) were actually considered for tube potentials ≤80 kVp. A strict implementation of BMI eligibility criteria with ≤80 kVp protocols for

patients with a BMI <25 kg/m^2 and 90 to 100 kVp protocols for patients with a BMI between 25 and 30 kg/m^2 would have lowered the median DLP of the PROTECTION VI population by 23% to 150 mGy × cm (interquartile range, 84 to 275 mGy × cm). A clinical practice guideline for the selection of tube potential protocols that includes these BMI eligibly criteria is illustrated in **Figure 4**.

STUDY LIMITATIONS. Although the diagnostic accuracy of CCTA with low and very-low tube potentials is high (25), the use of too strong iterative image reconstruction algorithms for counterbalancing image noise might result in too smoothened vessel delineation, which might result in concealing circumscriptive coronary stenosis. Although the delineation of the coronary artery lumen still appears feasible at 100 kVp tube potentials in patients with extensive coronary calcifications, the increased blooming artifacts of large calcified plaques might impair the diagnostic reading at very-low tube potentials. Thus, in elderly patients with a higher probability of extensive coronary calcifications, it might be helpful to estimate the burden of coronary calcification calcium scoring before CCTA with very-low tube potentials. Finally, the impact of very-low kVp scan protocols on coronary plaque quantification, on assessment of plaque composition, and on new CT technologies including CT-derived fractional flow reserve is currently unknown. Additional iterative reconstruction could have influenced the outcome parameters of the current study, however, only a very small fraction of low kVp scans was performed without iterative reconstruction. Statistical limitations are the lack of adjustments in patient characteristics for clustered observations between study sites.

CONCLUSIONS

This large international study demonstrates that a decrease of tube potential gradually improves patient safety by significantly reducing radiation dose and contrast agent volume. Low tube potential protocols are feasible in clinical routine and are noninferior regarding image quality, when compared with conventional tube potential imaging. This study also demonstrates that tube potential reduction has been increasingly implemented during the last decade. Especially moderate tube potential reduction between 90 kVp and 100 kVp has gained popularity in clinical routine. However, the current study also demonstrates the need for additional and escalated tube potential reduction. In particular, the application of very-low tube potential protocols ≤80 kVp should be considered in clinical practice.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: The clinical indications for CCTA imaging have significantly expanded during recent years and, likewise, the proportion of younger patients has increased. In this context, safety concerns in CCTA imaging and especially the exposure to potentially harmful radiation are increasingly recognized. Low tube potential imaging is a powerful method to lower radiation dose in eligible patients. Tube potential in CCTA imaging should be set as low as technically possible and reasonably achievable considering BMI eligibility criteria.

TRANSLATIONAL OUTLOOK: Training programs for CT operators are necessary to improve CCTA image protocols and increase the proportion of low tube potential scans. Further improvements of software with implementation of automated tube potential selection on the basis of patient characteristics including height and body weight may add to dose reduction. The application of quality control programs should be recommended to guide patients in the identification of expert centers following recommendations for dose reduction in CCTA imaging.

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KEY WORDS cardiac imaging, coronary computed tomography angiography, dose-saving strategies, radiation dose, tube potential

APPENDIX For a list of the PROTECTION VI Investigators as well as a supplemental table, please see the online version of this paper.