Application of low tube potentials in coronary CT angiography: Results from the PROTECTION VI study

Thomas J. Stocker, M.D.[a,b,*], **Jonathon Leipsic, M.D.**[c], **Martin Hadamitzky, M.D.**[d], **Marcus Y. Chen, M.D.**[e], **Ronen Rubinshtein, M.D.**[f], **Simon Deseive, M.D.**[g,b], **Mathias Heckner**[h], **Jeroen J. Bax, M.D., Ph.D.**[i], **Kakuya Kitagawa, M.D., Ph.D.**[j], **Hugo Marques, M.D.**[k], **Axel Schmermund, M.D.**[l], **Claudio Silva, M.D.**[m], **John Mahmarian, M.D.**[n], **Joon-Won Kang, M.D., Ph.D.**[o], **Erik L. Grove, M.D., Ph.D.**[p,q], **John Lesser, M.D.**[r], **Steffen Massberg, M.D.**[s,b], **Jörg Hausleiter, MD**[t,b,*]

[a]Medizinische Klinik und Poliklinik I, Ludwig Maximilians-Universität, Munich, Germany

[b]DZHK (German Center for Cardiovascular Research), Partner Site Munich Heart Alliance, Munich, Germany

[c]University of British Columbia, Vancouver, Canada

[d]Institut für Radiologie und Nuklearmedizin, Deutsches Herzzentrum München, Munich, Germany

[e]National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, United States

[f]Lady Davis Carmel Medical Center, Haifa, Israel

[g]Medizinische Klinik und Poliklinik I, Ludwig Maximilians-Universität, Munich, Germany

[h]Medizinische Klinik und Poliklinik I, Ludwig Maximilians-Universität, Munich, Germany

[i]Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands

[j]Mie University Hospital, Tsu, Japan

[k]UNICA (Cardiovascular imaging Unit), Hospital da Luz, Lisbon, Portugal

[l]Cardioangiologisches Centrum Bethanien, CCB, Frankfurt, Germany

[m]Radiology Department, Clinica Alemana de Santiago, Santiago, Chile

[n]Houston Methodist Hospital, Houston, United States

[o]Asan Medical Center, Seoul, South Korea

[p]Aarhus University Hospital, Aarhus, Denmark

[q]Department of Clinical Medicine, Faculty of Health, Aarhus University, Aarhus, Denmark

[*]**Address for correspondence:** Jörg Hausleiter, M.D., Medizinische Klinik und Poliklinik I, Klinikum der Universität München, Ludwig-Maximilians-Universität, Marchioninistrasse 15, 81377 Munich, Germany, Phone: +49-89-4400-72361, Fax: +49-89-4400-78788, joerg.hausleiter@med.uni-muenchen.de.

Clinical Trial Information: clinicaltrials.gov: NCT02996903

[r]Minneapolis Heart Institute, Minneapolis, United States

[s]Medizinische Klinik und Poliklinik I, Ludwig Maximilians-Universität, Munich, Germany

[t]Medizinische Klinik und Poliklinik I, Ludwig Maximilians-Universität, Munich, Germany

Abstract

Objectives: The aim of this study was to assess the utilization 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 employed 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 (90–100-kVp), conventional (110–120-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 to conventional tube potentials, low tube potentials were used in 56% of CCTAs (80-kVp: 9%; 90–100-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 90–100-kVp when compared to 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), while SNR and CNR significantly improved (both p<0.001). Considering BMI eligibility criteria, 58% (n=946) conventionally scanned patients would have been suitable for low tube potential protocols, and 44% (n=831) of patients scanned with 90–100-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 underutilized in daily practice.

Introduction

Coronary CT angiography (CCTA) has emerged as 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 non-fatal myocardial infarction (4). The downside of CCTA imaging is the adverse exposition 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 study (6). Reduction in tube potentials from the conventional 120 kVp is a major contributor to this dose reduction. Several studies demonstrated the feasibility of a reduced potential to 100 kVp with maintenance of image quality (7–10). Additional experimental studies with limited number of patients suggested very-low tube potentials down to 80 kVp or below 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 below 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 above 30 kg/m^2 has also been described, but only in small patient populations (16). An escalation of low tube potential imaging towards 80 kVp or below was proposed in several studies for patients with a BMI below 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 data sets 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 non-diagnostic image quality. Non-diagnostic 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 non-diagnostic when at least one coronary artery was of non-diagnostic image quality.

Estimation of radiation dose

The collected parameters relevant to radiation dose included the volume 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 x cm (21) or alternatively a proposed conversion factor for CCTA imaging $k = 0.026$ mSv/mGy x cm (22).

Statistical analysis

Variables are expressed as counts with percentages 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 non-parametric variables were conducted with the Kruskal-Wallis chi-squared test, subsequent post-hoc analysis was performed with the Dunn's 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 90–100 kVp (Figure 1). Conventional tube potential of 110–120 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 (Figure 1). Accordingly, the selection of reduced tube potential 100 kVp ranged from 0% to 100% of CCTAs in study sites. On the one end, five 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 2). Low tube potential protocols of 90–100 kVp were less frequently utilized with GE scanners (42% of CCTAs), when compared to 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 to 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 Supplementary Table S1.

Patient and scan characteristics for all 4 groups of tube potential protocols (80-kVp, 90–100-kVp, 110–120-kVp and 130-kVp) are summarized in Table 1. While 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 to 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. 110–120-kVp; p < 0.001), while the proportion of prospective scan techniques was similar (86% vs. 88% for 80-kVp vs. 110–120-kVp; p = 0.39).

Reduction of radiation dose and contrast agent in low tube potential CCTA

When using conventional tube potential (110–120 kVp), the median $CTDI_{vol}$ added up to 22.8 [13.2 to 34.4] mGy. Application of low tube potential protocols significantly lowered the median $CTDI_{vol}$ to 11.1 [6.3 to 16.6] mGy or 6.9 [2.8 to 10.6] mGy using 90–100 kVp or 80 kVp protocols, respectively (p < 0.001). The median DLP for conventional 110–120-kVp scanning resulted in 310 [182 to 468] mGy x cm and was reduced by 50% (156 [88 to 236] mGy x cm) or even 68% (98 [46 to 160] mGy x cm) with the use of 90–100 kVp or 80 kVp tube potential protocols (both p < 0.001; Figure 3A). Consequently, median radiation dose for conventional tube potential imaging was estimated to 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 90–100 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 110–120 kVp, median contrast agent volume added up to 80 [70 to 100] ml and could be reduced by 13% (70 [60 to 80] ml) or even 25% (60 [55 to 79] ml) using 90–100 kVp or 80 kVp protocols, respectively (p < 0.001; Figure 3B).

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 90–100 kVp or 80 kVp increased image noise by 6% or 23%, when compared to conventional 110–120 kVp CCTAs (both p < 0.001). However, the median SNR improved with tube potential reduction by 20% or 31% for 90–100 kVp or 80 kVp compared to 110–120 kVp scanning (both p < 0.001). Similarly, CNR improved by 25% or 39% with the utilization of 90–100-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, 90–100-kVp, 110–120-kVp and 130-kVp; 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 4A). The majority of patients had a BMI < 30 kg/m^2 (n = 2,940) and was eligible for the application of tube potential reduction. In fact, 67% of these patients were scanned with low tube potential protocols (90–100 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 (90–100 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 4B). In the conventional group without tube potential reduction (110–120 kVp), we identified 58% of patients (n = 946) with a BMI < 30 kg/m^2 that would have been eligible for tube potential reduction to at least 100 kVp. In the group of CCTAs performed with 90–100-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 non-invasive 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 x 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 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 utilization 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 below in clinical routine imaging. The utilization of very-low tube potentials of 80 kVp was associated with a reduction of the mean DLP by 68% compared to 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 90–100-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 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 decline 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 of 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 non-diagnostic 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 below 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 to 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, four 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. Secondly, 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, while on the other hand several study sites demonstrated that the majority of patients could be scanned with protocols of 80 kVp and below 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 below 25 kg/m^2) were actually considered for tube potentials 80 kVp. A strict implementation of BMI eligibility criteria with 80-kVp protocols for patients with a BMI below 25 kg/m^2 and 90–100-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 x cm (interquartile range 84 to 275 mGy x cm). A clinical practice guideline for the selection of tube potential protocols that includes these BMI eligibly criteria is illustrated in Figure 5.

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. While 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 non-inferior regarding image quality, when compared to 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Relationship with industry (conflict of interest statement and financial disclosure statement):

Appendix

PROTECTION VI Investigators (sorted by country)

1. Patricia Carrascosa and Alejandro Deviggiano, Diagnóstico Maipú, Buenos Aires, Argentina

2. Christopher Naoum and John Magnussen, Macquarie University Hospital, Sydney, Australia

3. James Otton and Anthony Kaplan, Spectrum Radiology Liverpool, Sydney, Australia

4. Gudrun Feuchtner and Fabian Plank, Medizinische Universität, Innsbruck, Austria

5. Kristof De Smet and Nico Buls, Universitair Ziekenhuis, Brussel, Belgium

6. Roberto Caldeira Cury and Marcio Sommer Bittencourt, Delboni / DASA, Sao Paulo, Brazil

7. Cesar Higa Nomura and Roberto Nery Dantas Junior, Heart Institute – InCor, Sao Paulo, Brazil

8. Jonathon Leipsic and Philipp Blanke, University of British Columbia, Vancouver, Canada

9. Carl Chartrand-Lefebvre and Anne Chin, University of Montreal, Montreal, Canada

10. Gary Small and Benjamin Chow, University of Ottawa Heart Institute, Ottawa, Canada

11. Claudio Silva F, Clinica Alemana de Santiago, Santiago, Chile

12. Marcelo Godoy Z. and Claudio Silva F., Clinica Alemana de Temuco, Temuco, Chile

13. Xiang-Ming Fang and Wang Jie, Wuxi People's Hospital, Wuxi, China

14. Alberto Cadena, Clínica de la Costa, Barranquilla, Colombia

15. Theodor Adla and Vojtech Suchanek, Motol University Hospital, Prague, Czech Republic

16. Erik Lerkevang Grove and Kamilla Bech Pedersen, Aarhus University Hospital, Aarhus, Denmark

17. Jess Lambrechtsen and Mirza Husic, OUH-Svendborg, Svendborg, Denmark

18. Juhani Knuuti and Teemu Maaniitty, Turku University Hospital, Turku, Finnland

19. Bernhard Bischoff and Elisabeth Arnoldi, Klinikum der Universität München, München, Germany

20. Axel Schmermund and Joachim Eckert, Cardioangiologisches Centrum Bethanien, Frankfurt, Germany

21. Martin Hadamitzky and Tom Finck, Deutsches Herzzentrum München, München, Germany

22. Michaela Hell and Mohamed Marwan, Universitätsklinikum Erlangen-Nürnberg, Erlangen, Germany

23. Fabian Bamberg and Stefanie Mangold, Universitätsklinikum Tübingen, Tübingen, Germany

24. Thomas Schlosser and Johannes Ludwig, Universitätsklinikum Essen, Essen, Germany

25. Maria Mylona and Spyros Skiadopoulos, Olympion Hospital, Patras, Greece

26. Pál Maurovich-Horvat and Bálint Szilveszter, MTA-SE Cardiovascular Imaging Research Group, Heart and Vascular Center, Budapest, Hungary

27. Uday Jadav and Brian V. Pinto, MGM New Bombay Hospital, Vashi New Mumbai, India

28. 28. Ronen Rubinshtein and Essam Hussein, Lady Davis Carmel Medical Center, Haifa, Israel

29. Daniele Andreini and Gianluca Pontone, Centro Cardiologico Monzino, Milan, Italy

30. Eugenio Martuscelli and Massimiliano Sperandio, Policlinico di Tor Vergata, Rome, Italy

31. Kakuya Kitagawa and Naoki Nagasawa, Mie University Hospital, Tsu, Japan

32. Ramzi Tabbalat and Rami A. Farhan, Khalidi Hospital, Amman, Jordan

33. Lilia M. Sierra Galán and Leovigildo A. Delgado, American British Cowdray Medical Center Observatory Campus, Mexico City, Mexico

34. Lilia M. Sierra Galán and Marco A. Reza Orozco, American British Cowdray Medical Center Santa Fe Campus, Mexico City, Mexico

35. Francisco C. Castellón and Mariana D. Zamudio, Instituto Ignacio Chavez, Mexico City, Mexico

36. Andres Preciado-Anaya and Rafael P. Gómez, Hospital Siena, Leon, Mexico

37. Signe Helene Forsdahl and Grete Anita Hansen, University Hospital North Norway, Tromsø, Norway

38. Anne Günther and Joanna F. Kristiansen, Oslo University Hospital Rikshospitalet, Oslo, Norway

39. Edith Chavez Huapalla and Percy Teran Chavez, Complejo Hospitalario San-Pablo, Surco, Peru

40. Hugo M. Rodrigues Marques and Pedro de A. Goncalves, UNICA (Cardiovascular imaging Unit), Hospital da Luz, Lisbon, Portugal

41. Subramaniyan Ramanathan, Al Wakra Hospital, Doha, Qatar

42. Valentin Sinitsyn and Maria Glazkova, Federal Center of Medicine and Rehabilitation, Moscow, Russia

43. Rami Abazid and Osama A. Smettei, Prince Sultan Cardiac Center, Burydah, Saudi Arabia

44. Ahmed Dawood and Salama Hussain Omar, Dr Erfan and Bagedo Hospital, Jeddah, Saudi Arabia

45. Joon-Won Kang and Dong Hyun Yang, Asan Medical Center, Seoul, South Korea

46. Tae Hoon Kim and Chul Hwan Park, Gangnam Severance Hospital, Seoul, South Korea

47. Sanghoon Shin and Seok Jong Ryu, Ilsan Hospital, Goyang-si, South Korea

48. Jose R. Palomares and Hug Cuellar, Hospital Val d'Hebron, Barcelona, Spain

49. Jeroen J. Bax and Alexander van Rosendael, Leiden University Medical Center, Leiden, Netherlands

50. Michelle C. Williams, David Newby and Edwin J. R. van Beek, University of Edinburgh, Edinburgh, United Kingdom

51. Russell Bull and Kavin Jayawardhana, Royal Bournemouth Hospital, Bournemouth, United Kingdom

52. Patricia Dickson and Jennifer Espey, Capital Cardiology Associates, Albany, United States

53. John Lesser, Minneapolis Heart Institute, Minneapolis, United States

54. Renée Bullock-Palmer, Deborah Heart and Lung Center, Browns Mills, United States

55. Mark Rabbat and Nancy Schoenecker, Loyola University Medical Center, Maywood, United States

56. Dustin M. Thomas and Rosco S. Gore, San Antonio Military Medical, San Antonio, United States

57. Melany Atkins, Fairfax Radiological Consultants, Fairfax, United States

58. Marcus Y. Chen and Sujata M. Shanbhag, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, United States

59. John Mahmarian, Houston Methodist Hospital, Houston, United States

60. Jeannie Yu, Long Beach VA Healthcare System, Long Beach, United States

61. Todd C. Villines and Binh Nguyen, Walter Reed National Military Medical Center, Bethesda, USA

Abbreviations list

CT	Computed tomography
CCTA	Coronary CT angiography
DLP	Dose-length product
BMI	Body mass index
SNR	Signal-to-noise ratio
CNR	Contrast-to-noise ratio

References

1. Williams MC, Hunter A, Shah ASVet al.Use of Coronary Computed Tomographic Angiography to Guide Management of Patients With Coronary Disease. J Am Coll Cardiol2016;67:1759–1768. [PubMed: 27081014]

2. Budoff MJ, Dowe D, Jollis JGet al.Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. J Am Coll Cardiol2008;52:1724–32. [PubMed: 19007693]

3. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. Lancet2015;385:2383–91. [PubMed: 25788230]

4. Newby DE, Adamson PD, Berry Cet al.Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. The New England journal of medicine2018;379:924–933. [PubMed: 30145934]

5. Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography. JAMA2007;298:317–23. [PubMed: 17635892]

6. Stocker TJ, Deseive S, Leipsic Jet al.Reduction in radiation exposure in cardiovascular computed tomography imaging: results from the PROspective multicenter registry on radiaTion dose Estimates of cardiac CT angIOgraphy iN daily practice in 2017 (PROTECTION VI). Eur Heart J2018;39:3715–3723. [PubMed: 30165629]

7. Bischoff B, Hein F, Meyer Tet al.Impact of a reduced tube voltage on CT angiography and radiation dose: results of the PROTECTION I study. JACC Cardiovasc Imaging2009;2:940–6. [PubMed: 19679281]

8. Leschka S, Stolzmann P, Schmid FTet al.Low kilovoltage cardiac dual-source CT: attenuation, noise, and radiation dose. Eur Radiol2008;18:1809–17. [PubMed: 18392829]

9. Hausleiter J, Meyer T, Hadamitzky Met al.Radiation dose estimates from cardiac multislice computed tomography in daily practice: impact of different scanning protocols on effective dose estimates. Circulation2006;113:1305–10. [PubMed: 16520411]

10. Sun G, Hou YB, Zhang Bet al.Application of low tube voltage coronary CT angiography with low-dose iodine contrast agent in patients with a BMI of 26–30 kg/m2. Clin Radiol2015;70:138–45. [PubMed: 25468636]

11. Wu Q, Wang Y, Kai Het al.Application of 80-kVp tube voltage, low-concentration contrast agent and iterative reconstruction in coronary CT angiography: evaluation of image quality and radiation dose. Int J Clin Pract2016;70Suppl 9B:B50–5. [PubMed: 27577515]

12. Mangold S, Wichmann JL, Schoepf UJet al.Automated tube voltage selection for radiation dose and contrast medium reduction at coronary CT angiography using 3(rd) generation dual-source CT. Eur Radiol2016;26:3608–16. [PubMed: 26847044]

13. Jun BR, Yong HS, Kang EY, Woo OH, Choi EJ. 64-slice coronary computed tomography angiography using low tube voltage of 80 kV in subjects with normal body mass indices: comparative study using 120 kV. Acta Radiol2012;53:1099–106. [PubMed: 23034796]

14. LaBounty TM, Leipsic J, Poulter Ret al.Coronary CT angiography of patients with a normal body mass index using 80 kVp versus 100 kVp: a prospective, multicenter, multivendor randomized trial. AJR Am J Roentgenol2011;197:W860–7. [PubMed: 22021533]

15. Liu S, Fu Q, Yu Het al.Evaluate of the effect of low tube voltage on the radiation dosage using 640-slice coronary CT angiography. J Xray Sci Technol2018;26:463–471. [PubMed: 29562576]

16. Pan YN, Li AJ, Chen XM, Wang J, Ren DW, Huang QL. Coronary Computed Tomographic Angiography at Low Concentration of Contrast Agent and Low Tube Voltage in Patients with Obesity:: A Feasibility Study. Acad Radiol2016;23:438–45. [PubMed: 26872868]

17. Zhang F, Yang L, Song Xet al.Feasibility study of low tube voltage (80 kVp) coronary CT angiography combined with contrast medium reduction using iterative model reconstruction (IMR) on standard BMI patients. Br J Radiol2016;89:20150766. [PubMed: 26607646]

18. Wang W, Zhao YE, Qi Let al.Prospectively ECG-triggered high-pitch coronary CT angiography at 70 kVp with 30mL contrast agent: An intraindividual comparison with sequential scanning at 120 kVp with 60mL contrast agent. Eur J Radiol2017;90:97–105. [PubMed: 28583653]

19. Stocker TJ, Deseive S, Chen Met al.Rationale and design of the worldwide prospective multicenter registry on radiation dose estimates of cardiac CT angiography in daily practice in 2017 (PROTECTION VI). J Cardiovasc Comput Tomogr2018;12:81–85. [PubMed: 29233632]

20. Hausleiter J, Meyer T, Hermann Fet al.Estimated radiation dose associated with cardiac CT angiography. JAMA2009;301:500–7. [PubMed: 19190314]

21. Shrimpton PC, Hillier MC, Lewis MA, Dunn M. National survey of doses from CT in the UK: 2003. Br J Radiol2006;79:968–80. [PubMed: 17213302]

22. Trattner S, Halliburton S, Thompson CMet al.Cardiac-Specific Conversion Factors to Estimate Radiation Effective Dose From Dose-Length Product in Computed Tomography. JACC Cardiovasc Imaging2018;11:64–74. [PubMed: 28823748]

23. Sigal-Cinqualbre AB, Hennequin R, Abada HT, Chen X, Paul JF. Low-kilovoltage multi-detector row chest CT in adults: feasibility and effect on image quality and iodine dose. Radiology2004;231:169–74. [PubMed: 15068946]

24. Piechowiak EI, Peter JF, Kleb B, Klose KJ, Heverhagen JT. Intravenous Iodinated Contrast Agents Amplify DNA Radiation Damage at CT. Radiology2015;275:692–7. [PubMed: 25654667]

25. Andreini D, Mushtaq S, Conte Eet al.Coronary CT angiography with 80 kV tube voltage and low iodine concentration contrast agent in patients with low body weight. J Cardiovasc Comput Tomogr2016;10:322–6. [PubMed: 27357327]
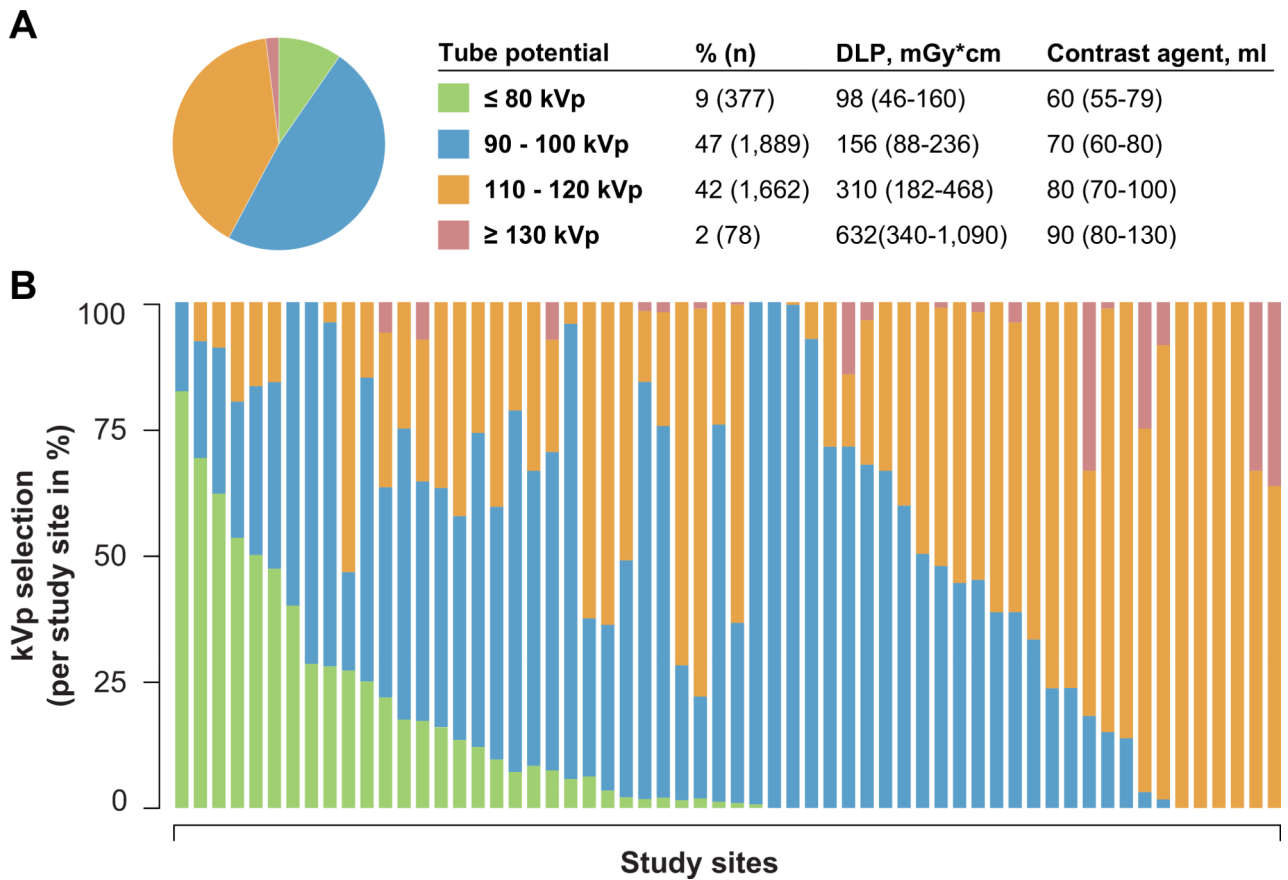
Perspectives

Clinical competencies (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.

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

Central illustration, Figure 1: Application of tube potential protocols in current clinical routine CCTA imaging.
A: Frequency of different tube potential protocols aggregated to 80-kVp, 90–100-kVp, 110–120-kVp and 130-kVp. **B:** Variation of tube potential protocol selection per study site.

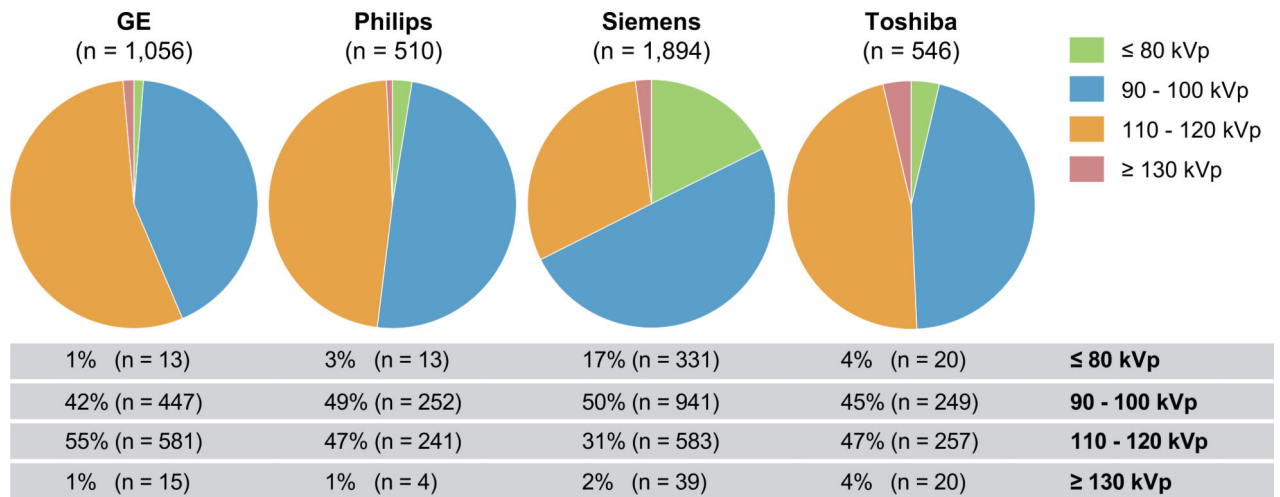| GE (n = 1,056)	Philips (n = 510)	Siemens (n = 1,894)	Toshiba (n = 546)	
1% (n = 13)	3% (n = 13)	17% (n = 331)	4% (n = 20)	**≤ 80 kVp**
42% (n = 447)	49% (n = 252)	50% (n = 941)	45% (n = 249)	**90 - 100 kVp**
55% (n = 581)	47% (n = 241)	31% (n = 583)	47% (n = 257)	**110 - 120 kVp**
1% (n = 15)	1% (n = 4)	2% (n = 39)	4% (n = 20)	**≥ 130 kVp**

Figure 2: Tube potential protocol selection by CT vendor.
GE: General Electric Healthcare, Waukesha, Wisconsin. Philips: Philips Healthcare, Amsterdam, Netherlands. Siemens: Siemens Medical Solutions, Forchheim, Germany. Toshiba: Toshiba Medical Systems Corporation,   tawara, Tochigi, Japan.
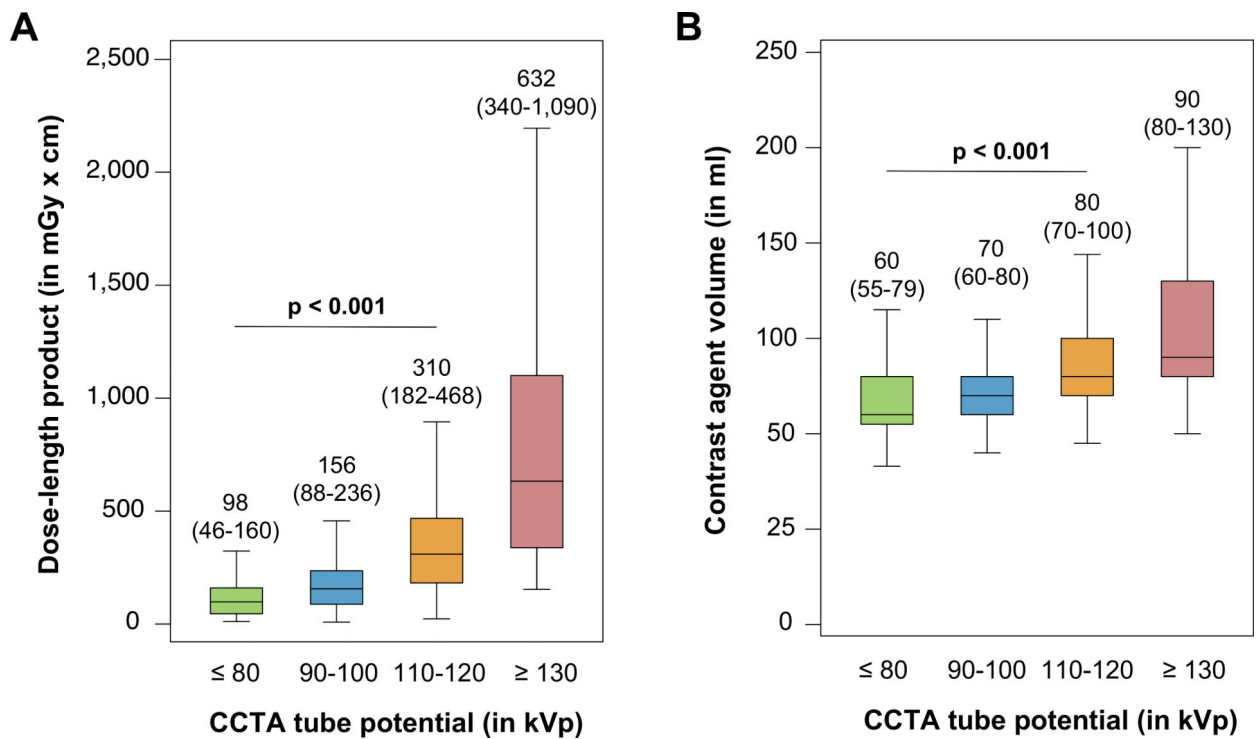
Figure 3: Impact of tube potential reduction on dose-length product and contrast agent volume in CCTA imaging.

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 interquartile range (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.

A

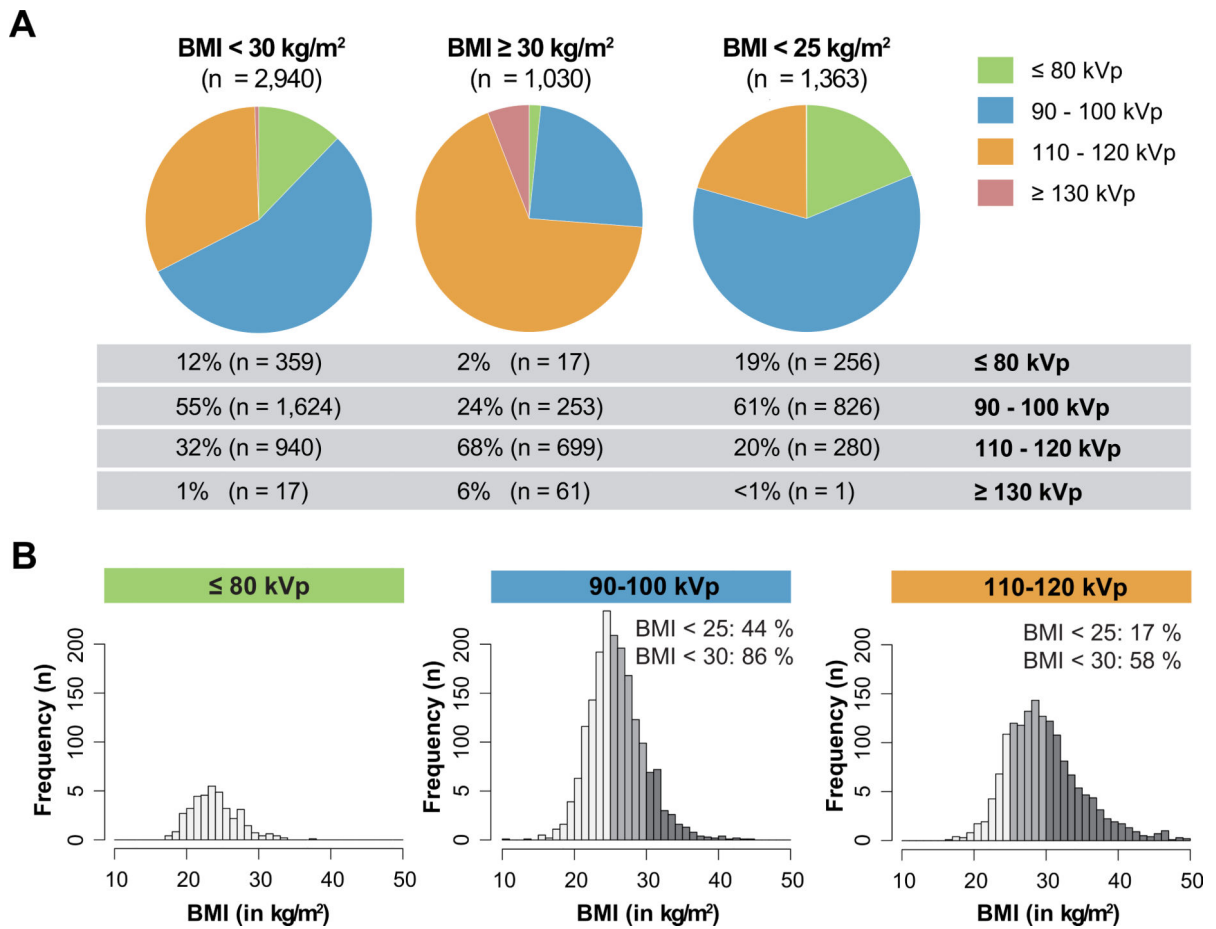|		
BMI < 30 kg/m² (n = 2,940)	**BMI ≥ 30 kg/m²** (n = 1,030)	**BMI < 25 kg/m²** (n = 1,363)

Legend:
- ≤ 80 kVp
- 90 - 100 kVp
- 110 - 120 kVp
- ≥ 130 kVp

12% (n = 359)	2% (n = 17)	19% (n = 256)	**≤ 80 kVp**
55% (n = 1,624)	24% (n = 253)	61% (n = 826)	**90 - 100 kVp**
32% (n = 940)	68% (n = 699)	20% (n = 280)	**110 - 120 kVp**
1% (n = 17)	6% (n = 61)	<1% (n = 1)	**≥ 130 kVp**

B

≤ 80 kVp	90-100 kVp	110-120 kVp
	BMI < 25: 44 % BMI < 30: 86 %	BMI < 25: 17 % BMI < 30: 58 %

Figure 4: 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 body mass index (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), 90–100-kVp (middle) and 110–120-kVp (right).
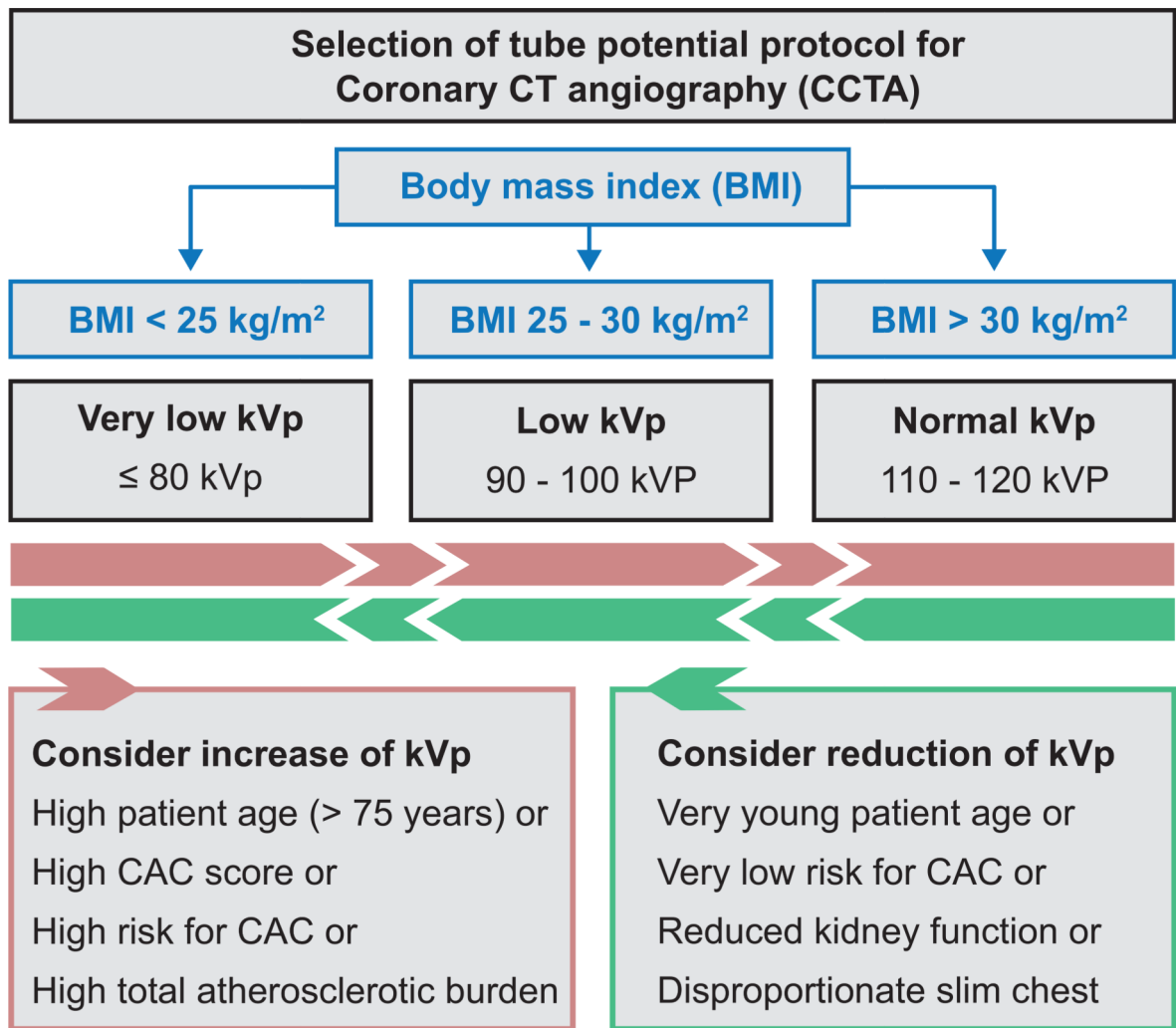
Figure 5: Clinical practice guideline for the selection of tube potential protocols in CCTA imaging.

Body mass index (BMI) eligibility criteria categorize the tube potential protocol. Additional factors may increase (red box) or reduce (green box) the ideal tube potential category. Coronary artery calcification (CAC).

Table 1:

Patient and CCTA scanning characteristics

	80 kVp (n = 377)	90–100 kVp (n = 1889)	110–120 kVp (n = 1662)	130 kVp (n = 78)	p value
Patient characteristics					
Age, years	61 (50–70)	59 (50–68)	59 (51–68)	59 (52–68)	0.71
Male sex, %	45 (166)	54 (1027)	63 (1048)	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 (1026)	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, years	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 (1526)	82 (1359)	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)	

Data are presented as % (n) or median (interquartile range). Body mass index (BMI).

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
Contrast-to-noise ratio (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
Signal-to-noise ratio (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 (1840)	97.8 (1524)	97.4 (76)	0.41

Data are presented as % (n) or median (interquartile range). HU = Hounsfield units.